

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

JOHN HANCOCK LIFE INSURANCE
COMPANY, JOHN HANCOCK
VARIABLE LIFE INSURANCE
COMPANY and MANULIFE
INSURANCE COMPANY,

Plaintiffs,

v.

ABBOTT LABORATORIES,

Defendant.

CIVIL ACTION NO. 05-11150-DPW

ABBOTT'S CORRECTED DEPOSITION DESIGNATIONS AND COUNTER-DESIGNATIONS FOR ANDREA LANDSBERG

Defendant Abbott Laboratories (“Abbott”) respectfully submits the attached corrected deposition designations and counter-designations for the February 16, 2007 deposition of Andrea Landsberg, Senior Manager, New Product Development (ABT-594).

Dated: February 22, 2008

Respectfully submitted,

ABBOTT LABORATORIES

By: /s/ Eric J. Lorenzini
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CERTIFICATE OF SERVICE

I hereby certify that this document(s) filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies will be sent to those indicated as non registered participants on February 22, 2008.

Date: February 22, 2008

/s/ Ozge Guzelsu

Andrea Landsberg Deposition Designations

Depo Date	Witness	Hancock Designation	Abbott Counter Designation	Abbott Designation	Deposition Exhibit	Plaintiff Exhibit	Defendant Exhibit
02/16/07	Landsberg, Andrea	4:6-4:7					
02/16/07	Landsberg, Andrea	5:17-6:3					
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02/16/07	Landsberg, Andrea			11:10-11:19			
02/16/07	Landsberg, Andrea	11:20-15:9					
02/16/07	Landsberg, Andrea	20:8-20:19					
02/16/07	Landsberg, Andrea	28:1-28:4					
02/16/07	Landsberg, Andrea			28:16-29:13			
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02/16/07	Landsberg, Andrea			32:20-33:10			
02/16/07	Landsberg, Andrea			33:19-34:4			
02/16/07	Landsberg, Andrea	47:7-47:21	47:22-48:6		4	SL	
02/16/07	Landsberg, Andrea			48:17-48:23			
02/16/07	Landsberg, Andrea			54:12-55:23			
02/16/07	Landsberg, Andrea	56:5-59:19			4	SL	

Depo Date	Witness	Hancock Designation	Abbott Counter Designation	Abbott Designation	Deposition Exhibit	Plaintiff Exhibit	Defendant Exhibit
02/16/07	Landsberg, Andrea	70:11-71:3			6	CO	
02/16/07	Landsberg, Andrea	72:23-73:3			6	CO	
02/16/07	Landsberg, Andrea	76:11-78:24	79:1-79:23		6	CO	
02/16/07	Landsberg, Andrea	80:16-82:4			6	CO	
02/16/07	Landsberg, Andrea	83:19-84:9			6	CO	
02/16/07	Landsberg, Andrea	85:14-85:23	85:24-86:7		6	CO	
02/16/07	Landsberg, Andrea			86:8-86:19			
02/16/07	Landsberg, Andrea	87:5-89:11	89:12-89:16		6	CO	
02/16/07	Landsberg, Andrea			99:9-100:2			
02/16/07	Landsberg, Andrea	104:13-106:12	106:13-106:18		10	SM	
02/16/07	Landsberg, Andrea	110:3-111:16			11	DG	
02/16/07	Landsberg, Andrea	116:4-116:20	116:21-118:15		11	DG	
02/16/07	Landsberg, Andrea	118:16-119:14			11	DG	
02/16/07	Landsberg, Andrea	142:19-142:24			18	DS	
02/16/07	Landsberg, Andrea	144:20-152:22			18 19	DS EB	
02/16/07	Landsberg, Andrea			154:19-155:16			
02/16/07	Landsberg, Andrea	180:11-181:21			26	EJ	
02/16/07	Landsberg, Andrea	183:22-184:8			26	EJ	

Depo Date	Witness	Hancock Designation	Abbott Counter Designation	Abbott Designation	Deposition Exhibit	Plaintiff Exhibit	Defendant Exhibit
02/16/07	Landsberg, Andrea	189:2-190:13			28	EL	
02/16/07	Landsberg, Andrea			191:4-191:17			
02/16/07	Landsberg, Andrea	194:17-194:20			28	EL	
02/16/07	Landsberg, Andrea	196:4-197:17			28	EL	
02/16/07	Landsberg, Andrea	202:11-202:18	202:19-203:19				
02/16/07	Landsberg, Andrea	203:20-206:20					
02/16/07	Landsberg, Andrea			208:7-208:16			
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02/16/07	Landsberg, Andrea			211:3-212:13			

Color Key to Deposition Designations

Designation by Plaintiffs

Counter Designation by Defendants

Designation by Defendants

Landsberg, Andrea (Linked) 2/16/2007 10:26:00 AM

1 IN THE UNITED STATES DISTRICT COURT
2 FOR THE DISTRICT OF MASSACHUSETTS
3 JOHN HANCOCK LIFE INSURANCE)
4 COMPANY, JOHN HANCOCK VARIABLE)
5 LIFE INSURANCE COMPANY, and)
6 MANULIFE INSURANCE COMPANY)
7 (f/k/a INVESTORS PARTNER)
8 INSURANCE COMPANY),)
9 Plaintiffs,) Civil Action No.

10 vs.) 05-11150-DPW

11 ABBOTT LABORATORIES,)

12 Defendant.)

13

14 The videotaped deposition of ANGELA

15 LANDSBERG, called for examination, taken pursuant to

16 the provisions of the Federal Rules of Civil

17 Procedure of the United States District Courts

18 pertaining to the taking of depositions for the

19 purpose of discovery, taken before Barbara J.

20 Cramer, CSR No. 84-1700, a Certified Shorthand

21 Reporter of the State of Illinois, at Suite 1300,

22 Two North LaSalle Street, Chicago, Illinois, on the

23 16th day of February, A.D. 2007, at 10:26 a.m.

24

Landsberg, Andrea (Linked) 02/16/2007 10:26:00 AM

1 MR. ELSEY: We are on the video record, yes.

2 ANDREA LANDSBERG,

3 called as a witness herein, having been first duly

4 sworn, was examined and testified as follows:

5 EXAMINATION

6 BY MR. DAVIS:

7 Q. Okay. Good morning.

8 A. Good morning.

9 Q. My name is Brian Davis. As you heard, I

10 represent John Hancock and the other plaintiffs in

11 this matter.

12 A. Um-hmm.

13 Q. First, let me apologize for the delay.

14 Unfortunately, the weather was not cooperating with

15 the shipments of the documents --

16 A. Um-hmm.

17 Q. -- that we needed for this deposition, so

18 I apologize for holding you up.

19 Now, what I'd like to do is ask you a

20 series of questions here today. If at any point in

21 time, Ms. Landsberg, you don't understand my

22 questions --

23 A. Um-hmm.

24 Q. -- please say so --

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1 A. Um-hmm.

2 Q. -- and I'll try to give you a clearer
3 question. Is that acceptable?

4 A. Yes.

5 Q. All right. In addition, as we go through
6 the deposition here today, you -- you do need to
7 verbalize your responses for the reporter. She
8 can't record head shakes or nods. So you have to
9 say yes or no or whatever is appropriate.

10 Do you understand that?

11 A. I understand.

12 Q. And if at any point in time you wish to
13 take a break, please let me know, and we'll try to
14 accommodate you as soon as possible thereafter. All
15 right?

16 A. All right.

17 Q. Would you state your full name for the
18 record, please?

19 A. Yes. Andrea Landsberg.

20 Q. Where do you live, Ms. Landsberg?

21 A. The whole address?

22 Q. Yes, please.

23 A. 23494 Eagles Nest Road, Antioch,
24 Illinois, 60002.

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1 Q. Where do you work?

2 A. Abbott Laboratories. I should say

3 "Abbott" now is our correct name.

4 Q. Okay. We'll have to revise the
5 pleadings.6 MR. LORENZINI: You'll have to revise the
7 pleadings.

8 BY THE WITNESS:

9 A. Sorry. I -- we're supposed to stop
10 saying the "Laboratories."11 MR. LORENZINI: It's the -- it's the Abbott
12 Laboratories in the court documents, so --

13 BY THE WITNESS:

14 A. Fine. So -- that's fine.

15 BY MR. DAVIS:

16 Q. We'll make all -- all the changes
17 necessary.

18 How long have you worked for Abbott?

19 A. It's about ten and a half years.

20 Q. What -- what position do you currently
21 hold at Abbott?22 A. General manager, primary care and
23 emerging markets for Abbott International.

24 Q. Is that a -- do you work within a

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1 particular division of Abbott?

2 A. Yes, Abbott International Division.

3 Q. What is the business of Abbott

4 International?

5 A. Pharmaceuticals, marketing and sales of

6 pharmaceuticals outside of the US.

7 Q. Is it fair to say that your job focuses

8 primarily on marketing and sales?

9 A. Yes.

10 Q. Has that been true all of time that

11 you've worked for Abbott in one capacity or another?

12 A. I'm running through all of my jobs in my

13 head. Yes.

14 Q. Are you -- is your office at Abbott Park?

15 A. Yes, it is.

16 Q. Briefly, what's your educational

17 background?

18 A. I have a B.S. in biology from Cook

19 College, Rutgers University. I have a V.M.D. from

20 University of Pennsylvania, and I have an M.B.A.

21 from Morgan, University of Pennsylvania, in that

22 order. I know; doctorate before the Master's.

23 Q. I'm sorry. What was the doctorate in?

24 A. Veterinary medicine.

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1 Q. What year did you obtain the B.S. from

2 Rutgers?

3 A. '84.

4 Q. When did you obtain the doctorate?

5 A. '88.

6 Q. And when did you obtain the M.B.A.?

7 A. '96.

8 Q. Did you go to work for Abbott for the

9 first time after you obtained your M.B.A.?

10 A. Yes.

11 Q. Had you worked prior to that?

12 A. Yes, as a veterinarian.

13 Q. Briefly, what are the positions that

14 you've held at Abbott, as best you recall, since you

15 joined them about ten years ago?

16 A. Excuse me. Initially on the management

17 development program, a series of positions, market

18 research analyst, sales representative, and then

19 associate product manager. I can define all the

20 products if you need that detail or -- or not.

21 Then continued as a product manager, then

22 a senior product manager, then a senior manager in

23 new product development, and then director of what

24 we called at the time professional communications.

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1 It is a marketing operations group.

2 Q. What was the position again? I'm sorry.

3 A. Director of professional communications

4 was its formal title. We ended up changing the

5 name, because it didn't reflect what it -- I forgot

6 what we changed its name to.

7 Q. Okay.

8 A. But it's basically a marketing operations

9 group, supports the marketing functions.

10 And then director for cardiovascular

11 products, and then was called both senior director

12 and then we changed it to a general manager, and the

13 final title was the general manager of the

14 commercial strategic initiatives, a combined sales

15 and marketing excellence role.

16 Q. Any others?

17 A. And then the one that I currently have.

18 Q. When did you take the position -- when

19 did you first assume the position that you're

20 currently in?

21 A. In July of this past year.

22 Q. At some time or another during the course

23 of your tenure at Abbott, you had some involvement

24 in the development of a compound named 594. Is that

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1 right?

2 A. Yes.

3 Q. Okay. That's ABT-594. Do you agree with

4 that?

5 A. Yes.

6 Q. And if I refer to it as 594, in the

7 course of your deposition, you'll understand that

8 I'm referring to ABT-594. Is that fair?

9 A. Yes.

10 Q. All right. In which of these positions

11 did you have any responsibility for ABT-594?

12 A. It was the senior manager, new product

13 development.

14 Q. And how long did you hold that position?

15 A. Only about seven months.

16 Q. Do you recall what seven months those

17 were?

18 A. Yeah, I've been trying to think of that.

19 I know I moved into that next position in February

20 of '01, so I'm thinking it must have been June of

21 2000 when I began that position, roughly.

22 Q. And the next position that you moved into

23 was the director of professional communications?

24 A. Yes.

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1 Q. When you became director of professional
2 communications, did your responsibilities for
3 ABT-594 cease?

4 A. Yes.

5 Q. Who took over responsi- -- the
6 responsibilities that you had had up to that point
7 in time for ABT-594 when you took that new position
8 in February of '02 -- '01?

9 A. I -- I don't recall.

10 Q. When did you first have any
11 responsibility for ABT-594?

12 A. It was probably as soon as I began in
13 that position, which I took over from Jim Doran, so
14 assumed all of his responsibilities.

15 Q. So that was approximately June of 2000?

16 A. Yes.

17 Q. Had you had any responsibility for
18 ABT-594 prior to that date?

19 A. No.

20 Q. So it's fair to say that all of your
21 involvement with respect to ABT-594 occurred in the
22 period from June of 2000 through -- to February --
23 sometime in February of '01.

24 A. To the best of my recollection, those

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1 dates, to the best of my recollection.

2 Q. And what responsibilities did you have
3 with respect to ABT-594?

4 A. It was a role that was designed to
5 provide commercial forecasting and support for any
6 of our pipeline products for, you know, discovery or
7 development products.

8 Q. Okay.

9 A. And I had two areas of responsibility.

10 Q. All right. Is it correct that at the
11 time that you first had any responsibility for 594,
12 that 594 already was under development by Abbott?

13 A. Yes.

14 Q. Were you part of some sort of team that
15 was focused on the development of ABT-594?

16 A. Yes.

17 Q. What was the name of the team?

18 A. I don't remember specifically what it was
19 called.

20 Q. Is it fair to say that your
21 responsibility on the team was to help provide the
22 sort of commercial and marketing support for the
23 development of ABT-594?

24 A. By support, I'm not sure. I mean, that

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1 can be very general, but ...

2 Q. I can be more specific. ABT-594 hadn't

3 been introduced to the market at that point in time.

4 Correct?

5 A. Correct.

6 Q. Part of your responsibilities were

7 helping to formulate plans, put together

8 projections, forecasts of that nature that could be

9 utilized by Abbott in deciding whether to introduce

10 ABT-594 and what steps to take in the event that it

11 was introduced. Is that fair to say?

12 MR. LORENZINI: Objection.

13 You can answer.

14 BY THE WITNESS:

15 A. I would say it was to develop the

16 forecasts. Anything that we had in development we

17 would have assumed we would continue to promote. I

18 was developing the plan for the launch of the

19 product.

20 BY MR. DAVIS:

21 Q. And part of developing the plan included

22 forecasting potential sales of the product. Is that

23 right?

24 A. Yes, it did.

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1 Q. Who else do you recall working with on

2 that team that was focused on ABT-594?

3 A. On the clinical team, Chris Silber and

4 Bruce McCarthy. And Laura -- and her last name is

5 escaping me -- was my Abbott International

6 counterpart.

7 Q. Laura Robinson?

8 A. Yes. Thank you. Laura Robinson.

9 Q. Who else?

10 A. There was a project team -- I -- I don't

11 know what his name was. He was sort of the -- we

12 call them now sort of project team leaders, so I

13 don't know what his exact title would have been back

14 then. But Mike --

15 Q. Biarnesen?

16 A. -- Biarnesen, yes.

17 Q. All right.

18 A. There were other people, but --

19 Q. All right.

20 A. The only other one I -- I can name is Jim

21 Sullivan, who was in the discovery team.

22 Q. Approximately how many people were on the

23 team all told?

24 MR. LORENZINI: Objection; vague.

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1 BY THE WITNESS:

2 A. I -- I -- it would be making a guess. I

3 don't remember. You know, a group of more than the

4 people I have named.

5 BY MR. DAVIS:

6 Q. Somewhere between --

7 A. It's safe to say there are some others.

8 Q. Is it somewhere between 10 and 20 people?

9 A. Yes, probably.

10 Q. How frequently did the team meet?

11 MR. LORENZINI: Objection; vague.

12 BY MR. DAVIS:

13 Q. We're talking about a period -- were you

14 on that -- well, let me go back for a second and

15 we'll try to address Mr. Lorenzini's objections.

16 Were you a member of the 594 team from

17 June of 2000 through February of 2001?

18 MR. LORENZINI: Objection.

19 You can answer.

20 BY THE WITNESS:

21 A. I don't remember my first meeting on 594,

22 when that was, you know, whether that was the first

23 week I took the job or a month or two into the job.

24

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1 I just want to make sure -- that your job was to

2 help develop sort of the -- the marketing plan for

3 the ABT-594?

4 A. By "marketing plan" -- yes, we did have

5 marketing plan development, and that would mean you

6 would be looking at what types of sales force you

7 would need to promote the brand.

8 Q. Let me -- let me go back for a moment. I

9 just want to make sure I have it clear on the

10 record. What was your role on the ABT-594 team?

11 A. To be the individual who would develop

12 the market forecasts for the product -- or, at this

13 point, compound -- and begin to plan for what a

14 launch would look like, so a preliminary market

15 plan; not as detailed as you would certainly have on

16 an on-market product for its market plan.

17 Q. Did you have any other responsibilities,

18 as best you recall?

19 A. No.

20 MR. DAVIS: Let's mark this as the first

21 exhibit, please. This will be Landsberg 1.

22 THE WITNESS: Is that mine?

23 MR. LORENZINI: She's got to put a sticker on

24 it.

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1 Q. While you were working on the 594 team,
2 were you aware that there was a Phase IIb clinical
3 study for neuropathic pain under way?

4 A. Yes.

5 Q. If you look at the fourth page of this
6 document under "Other Updates," do you see it says,
7 "Marilyn Collicott provided an update on the
8 M99-114," paren "neuropathic pain," close paren,
9 "study."

10 Do you see that?

11 A. Yes, I do.

12 Q. Is that the Phase IIb study that you
13 recall being under way?

14 A. I would not have recalled the number,
15 but, obviously, it is.

16 Q. All right. Did you -- while you were
17 working on the 594 team, did you receive information
18 regarding that particular study?

19 A. I can't say that I recall that
20 specifically or generally.

21 Q. It says here, "Currently, we have 99
22 subjects randomized with an approximate 50 percent
23 screen failure rate."

24 Do you recall any discussions or

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1 communications within Abbott on that topic?

2 MR. LORENZINI: Objection; vague.

3 You can answer.

4 BY THE WITNESS:

5 A. Not that I recall right now, no. But ...

6 BY MR. DAVIS:

7 Q. But ...

8 A. Yeah. I don't know, I was going to say.

9 Q. It says, "Our goal of enrollment is 320

10 subjects."

11 Do you recall that the targeted

12 enrollment for that study was 320 subjects?

13 A. No.

14 Q. It says, "There has been much concern

15 with the drop-out rate."

16 Do you see that?

17 A. Yes, I do.

18 Q. What is your recollection regarding the

19 concerns that were expressed regarding the drop-out

20 rate in that study?

21 MR. LORENZINI: Objection; lacks foundation.

22 BY THE WITNESS:

23 A. My recollection --

24 MR. LORENZINI: If any.

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1 BY THE WITNESS:

2 A. That's -- I don't have a personal
3 recollection of that.

4 BY MR. DAVIS:

5 Q. As you sit here today, you have no
6 recollection of any concerns being expressed
7 regarding the drop-out rate in that study?8 A. I -- I don't have any of my own
9 recollections. I see it here.10 Q. If you take a look at the first page
11 again of Exhibit 1, it lists you as an attendee at
12 this meeting.

13 Do you see that?

14 A. Yes, I see that.

15 Q. Do you have any reason to doubt that you
16 attended this meeting back in August of -- of 2000?

17 A. No, I do not.

18 Q. On -- so as you sit here today, can you
19 shed any light on why it is that these meeting
20 minutes indicate that there was much concern with
21 the drop-out rate at Abbott back in that time frame?22 MR. LORENZINI: Objection; vague. Are you
23 asking her to interpret reading this --

24 MR. DAVIS: No.

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1 trial causing much concern at that time?

2 MR. LORENZINI: Objection; lacks foundation.

3 BY THE WITNESS:

4 A. I can't say what the concern was besides
5 knowing that we -- obviously -- or speculating here
6 that we might have been off of our target on the
7 patients.

8 BY MR. DAVIS:

9 Q. What was the drop-out rate in the 114
10 study --

11 A. I --

12 Q. -- of the neuropathic pain trial as of
13 August 2000?

14 A. I don't recall.

15 Q. Was it an unusual drop-out rate?

16 MR. LORENZINI: Objection; vague.

17 BY THE WITNESS:

18 A. I don't know.

19 BY MR. DAVIS:

20 Q. Okay. Do you recall any discussions with
21 anyone in Abbott -- within Abbott in the summer of
22 2000 regarding the drop-out rate that was being
23 observed in the 114 study?

24 A. No.

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1 Q. And you agree that when I refer to the
2 "114 study," I'm referring to the Phase IIb
3 neuropathic pain trial. You understand that.

4 A. I understand.

5 Q. Did you get any preliminary data
6 regarding that 114 study while that study was
7 under -- under way?

8 MR. LORENZINI: Objection; vague.

9 BY THE WITNESS:

10 A. I have no recollection of that.

11 BY MR. DAVIS:

12 Q. Do you recall receiving any data
13 regarding adverse events that were being observed in
14 the 114 study while that study was under way?

15 MR. LORENZINI: Objection; vague and ambiguous.

16 BY THE WITNESS:

17 A. I need you to repeat that, just because I
18 lost that.

19 MR. DAVIS: Sure. Would you re-read the
20 question, please?

21 (WHEREUPON, the record was read by
22 the reporter.)

23 BY THE WITNESS:

24 A. I have no personal recollection.

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1 BY MR. DAVIS:

2 Q. You say you have no personal
3 recollection, meaning that you have no recollection.

4 A. I have no recollection.

5 MR. DAVIS: Let's mark this, please, as the
6 next exhibit.7 (WHEREUPON, a certain document was
8 marked Landsberg Deposition Exhibit
9 No. 2, for identification, as of
10 2/16/07.)

11 MR. LORENZINI: That's fine.

12 BY MR. DAVIS:

13 Q. Ms. Landsberg, you have in front of you
14 what's been marked as Exhibit 2, which appears to be
15 another set of minutes for a meeting on Tuesday,
16 August 1, 2000, although if you'd like to compare
17 the two, I think you'll see that there seems to be
18 different information in these minutes. Maybe it
19 was a --

20 A. Hmm.

21 Q. -- two meetings held at the same time on
22 the same day involving the same people, which sounds
23 a little farfetched, or there may simply be a
24 mistake on the date.

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1 teams that were responsible in any way for ABT-594?

2 MR. LORENZINI: Objection; vague and ambiguous.

3 BY THE WITNESS:

4 A. No.

5 MR. DAVIS: Let's mark this as the next

6 exhibit, please.

7 (WHEREUPON, a certain document was

8 marked Landsberg Deposition Exhibit

9 No. 4, for identification, as of

10 2/16/07.)

11 BY MR. DAVIS:

12 Q. Ms. Landsberg, you have what's been

13 marked as Exhibit 4. Would you look at this

14 document for a moment and tell me if you've ever

15 seen it before?

16 MR. LORENZINI: Objection; instruct the witness

17 not to answer to the extent the question in- --

18 includes seeing the document during our meeting.

19 BY THE WITNESS:

20 A. I do not, in any way, remember seeing

21 this before.

22 BY MR. DAVIS:

23 Q. All right. The first page appears to be

24 an email from you to Bruce McCarthy, Chris Silber,

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1 and Mike Biarnesen.

2 Do you see that?

3 A. Yes, I do.

4 Q. Do you have any reason to doubt that you
5 actually sent this email back in August of 2000?

6 A. No, no reason to doubt.

7 Q. Would you look briefly to the exit or the
8 attachment to this email?

9 A. I'm sorry. I'm just -- can I just finish
10 reading the note?

11 Q. Certainly.

12 A. Okay. Now, I'm sorry? Which page?

13 Q. The first -- the email itself is titled
14 under the subject "594 Development Plan."

15 Do you see that?

16 A. Yes, I do.

17 Q. Did you participate in the creation of a
18 development plan for ABT-594?

19 A. Yes.

20 Q. And what role did you have in the
21 creation of that development plan?

22 A. I would have provided the commercial
23 sections of the plan.

24 Q. If you take a look at the materials that

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1 reason to believe, as of August 2000, that adverse
2 events for ABT-594 were too frequent?

3 MR. LORENZINI: Objection; vague, ambiguous.

4 BY THE WITNESS:

5 A. I -- I'm sorry. I missed how you said
6 that, so I don't know which way to answer.

7 BY MR. DAVIS:

8 Q. Let me ask you again.

9 A. I don't know what the question is.

10 Q. You make -- you make reference in this
11 document to "If AEs for ABT-594 too frequent."

12 My question is: Did you have any reason
13 to believe in August of 2000 that adverse events and
14 the use of -- that resulted from the use of ABT-594
15 were too frequent?

16 MR. LORENZINI: Objection.

17 BY THE WITNESS:

18 A. I don't believe I would have -- I mean,
19 even looking at this, our first option is sell on
20 convenience, tolerability, and safety; so, no.

21 BY MR. DAVIS:

22 Q. If you look at the next box over under
23 strengths --

24 A. Um-hmm.

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1 Q. -- the second line says, "May be better

2 fit with AE profile."

3 Do you see that?

4 A. Yes, I do.

5 Q. What do you mean -- what was the AE

6 profile of ABT-594 as of August 2000?

7 MR. LORENZINI: Objection; vague and ambiguous,

8 lacks foundation.

9 BY THE WITNESS:

10 A. Anything that would have come from the

11 prior clinical research, the research that was

12 completed.

13 BY MR. DAVIS:

14 Q. Do you recall what the AE profile was for

15 ABT-594 with respect to nausea, vomiting, and

16 dizziness, as of August of 2000?

17 A. No.

18 Q. Do you recall any concerns being

19 expressed within Abbott in the summer of 2000

20 regarding the AE profile for ABT-594?

21 MR. LORENZINI: Objection; vague and ambiguous.

22 BY THE WITNESS:

23 A. No.

24

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1 BY MR. DAVIS:

2 Q. Would you turn, please, to the pages

3 Bates number ends in 9833?

4 A. Um-hmm.

5 Q. Do you see there's a table there entitled

6 "US Forecast, Date of Forecast, 7/00"?

7 A. Yes.

8 Q. What is -- what is that a U.S. forecast

9 of?

10 A. I would assume it's the forecast for 594,
11 since it's in the 594 document.12 Q. Um-hmm. Where did the information
13 contained in this table come from?14 A. Specifically the information that is here
15 right now, I couldn't tell you.16 Q. All right. Where did you typically
17 obtain this kind of information?18 A. This would have been developed -- and
19 these specific numbers would have been developed
20 either by my predecessor or myself. That's what I
21 don't know, who developed these numbers that are
22 sitting here on this table.23 Q. How would you go about developing these
24 numbers or numbers like these?

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1 A. For any forecast that was done, you would
2 do research on the disease state you were looking
3 at, by reviewing a number of sources. We had both
4 large -- we called them syndicated studies, I think,
5 of companies that put them out, like Decision
6 Resources or Data Monitor.

7 We would purchase those and look at what
8 they said the trends of patient population for the
9 target audience that you were looking at. And they
10 usually have projections over time. So you would
11 start there, kind of, what is my potential patient
12 base for the indication that you're looking at for a
13 product.

14 We could also -- we had access to a
15 number of databases -- I'm not remembering their
16 names -- but -- that have pipeline -- other
17 companies, their compounds that were in discovery or
18 development phases. We would also look at data that
19 we would pull from an IMS source. That's a company
20 that provides data on existing marketed products.

21 So you would take a look at what the existing
22 pattern was.

23 They have information on diagnosis codes
24 for reimbursement and how -- so what a particular

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1 product might be prescribe for. I'm getting into
2 more detail than you probably want.
3 But you -- but you take a lot of
4 different sources and come up with your market
5 assessment, you know, that it starts, usually, at
6 this point, with unmarketed products or products
7 that are not on the market yet. You almost always,
8 in my experience, do a patient based forecast.
9 That's why I'm saying you go back to the patient
10 population.
11 Then you look at potential rates of
12 diagnosis. Then you look of everybody who's
13 diagnosed, what are treated, percent of population
14 that might be treated. And then you get into your
15 assessment of your competitive set. So what is out
16 there now and how are they performing, what is out
17 there -- what is potential to come out, and what do
18 analysts say, what do the opinion leaders say, and
19 we look at everything you have and make a judgment
20 based on where you think your product will fit to
21 come up with a market prescription in the end.
22 There's usually a big spreadsheet analysis that you
23 do on this to get this -- these numbers.
24 Q. Okay. It sounds like a fair amount of

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1 work associated with this.

2 A. Yes.

3 Q. Okay. And what -- for what reason were
4 these forecasts prepared?

5 A. The reason of knowing whether you should
6 invest in a product. I mean, these are -- this
7 comes back to that portfolio planning process.

8 Where -- what do you think your future stream of
9 revenue will be --

10 Q. Is it your understanding that --

11 A. -- for a compound.

12 Q. -- the data was -- was prepared for the
13 purpose of assisting people within Abbott making
14 intelligent decisions about particular compounds?

15 A. Yeah, that's fair.

16 Q. And in preparing information like this,
17 was it your intention to try to make it as
18 reasonably accurate as you could?

19 A. Of course.

20 Q. And to your knowledge, was information --
21 were -- excuse me. To your knowledge, were
22 forecasts like this actually utilized by people
23 within Abbott for purposes of decision-making for
24 particular compounds, including 594?

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1 MR. DAVIS: We'll take a five-minute break, if
2 that's all right.

3 MR. ELSEY: All right. Going off the video
4 record at 11:37 a.m.

5 (WHEREUPON, a recess was had from
6 11:37 a.m. until 11:45 a.m.)

7 MR. ELSEY: And we are back on the video record
8 at 11:45 a.m. This is tape 2.

9 MR. DAVIS: Would you mark this, please, as the
10 next exhibit? We're up to 6.

11 (WHEREUPON, a certain document was
12 marked Landsberg Deposition Exhibit
13 No. 6, for identification, as of
14 2/16/07.)

15 BY MR. DAVIS:

16 Q. Ms. Landsberg, would you take a moment
17 and look at the document that has been marked as
18 Exhibit 6? In fact, what I'm going to ask you to do
19 is to take a few moments and read the emails --

20 A. Um-hmm.

21 Q. -- that form the first three pages of
22 Exhibit 6, and then please tell me when you're done
23 reading.

24 A. Okay.

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1 Q. Do you remember this exchange of email

2 correspondence back in August of 2000?

3 A. I don't.

4 Q. Do you recall that the drafts of the

5 commercial sections of the 594 development plan were

6 circulated among various people working on the 594

7 development team?

8 A. Do I remember that?

9 Q. Yes.

10 A. No.

11 Q. Does that shock you?

12 A. No.

13 Q. Is that consistent with the practice, as

14 best you recall at that time?

15 A. Is what consistent exactly --

16 Q. That you --

17 A. -- sharing it with who?

18 Q. That you would circulate drafts of the

19 commercial sections of the development plan for

20 ABT-594 with other people working on the development

21 team.

22 MR. LORENZINI: Objection; vague and ambiguous

23 as to which other people.

24

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1 BY MR. DAVIS:

2 Q. Any other people.

3 A. People who had knowledge that could help,

4 I assume.

5 Q. For example --

6 A. It might be possible.

7 Q. -- Mr. Biarnesen. Is it -- is it

8 consistent --

9 A. No.

10 Q. -- with your recollection that

11 Mr. Biarnesen would receive drafts of the portion --

12 commercial portions of the 594 development plan?

13 A. I would believe he would receive portions

14 because he was probably responsible for putting it

15 together, not that he was a clinical person, per se.

16 Q. But it's consistent with your

17 recollection that, because he was assembling the

18 document, he might receive drafts of the sections.

19 Is that right?

20 A. I don't have recollection, so I would say

21 it would be more consistent with what would be

22 typical in this type of situation.

23 Q. Well, do you have any reason to believe,

24 as you sit here today, that these email messages

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1 were not exchanged among you and others at Abb- --

2 in Abbott in August of 2000?

3 A. No.

4 Q. I think the email chain actually

5 begins --

6 A. Yeah.

7 Q. -- on the third page with Laura

8 Robinson's email to you and to Mr. Biarnesen.

9 Do you see that?

10 A. Yes.

11 Q. And one of the things that Ms. Robinson

12 says in that email in the second paragraph is "The

13 only issue I have is that we still seem to be

14 overpromising on the profile for ABT-594 regarding

15 tolerability."

16 Do you see that?

17 A. Yes.

18 Q. The reference to tolerability there, do

19 you understand that to be a reference to the

20 susceptibility of -- of ABT-594 to adverse events,

21 such as nausea, vomiting, and dizziness?

22 A. It would be tolerability overall.

23 Q. Would that include adverse events, such

24 as nausea, vomiting, and dizziness?

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1 same day you responded to Mr. Biarnesen's email, an
2 email that you sent on August 21, at approximately
3 10:56 a.m.

4 Do you see that?

5 A. Yes, I do.

6 Q. And in your email, you directed to
7 Mr. Biarnesen and Dr. McCarthy and Ms. --
8 Ms. Robinson.

9 Do you see that?

10 A. Yes.

11 Q. And one of the things that you state in
12 your email, if you look about two-thirds of the way
13 down your email, you see a paragraph that begins
14 "Forecast assumptions."

15 A. Yes, I see that.

16 Q. And in that paragraph, one of the things
17 you say is that "I'm using this here to be sure we
18 stay very aware of just how important this issue of
19 tolerability is to gain any market share."

20 Do you see that?

21 A. Yes.

22 Q. Now, actually, I should go back. In
23 that -- and that paragraph begins "Forecast
24 assumptions, again, not taking tolerability and

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1 safety, to only be applying just to V&N."

2 Do you see that?

3 A. Yes, I do.

4 Q. That V&N, is that a reference to vomiting

5 and nausea?

6 A. Yes, I believe so.

7 Q. And then later on, you say, in the same

8 paragraph, "I'm using this here to be sure we stay

9 very aware of just how important this issue of

10 tolerability is to gain any market share. I also

11 thought that we were assuming the current trial with

12 titration was supposed to greatly reduce the N&V

13 issue," paren, "Please let me know if this is a

14 misunderstanding on my part," close paren.

15 Let me stop there.

16 A. Um-hmm.

17 Q. Now, the reference to N&V there is to

18 nausea and vomiting. Is that right?

19 A. Yes, I believe so.

20 Q. And what was the nausea and vomiting

21 issue associated with ABT-594 as of August 2000?

22 A. I don't recall specifically. I don't

23 recall in general. I'm sorry. I don't recall. I

24 don't recall.

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1 Q. And when you say, "We were -- we were
2 assuming the current trial with titration was
3 supposed to greatly reduce the nausea and vomiting
4 issue," are you referring to the 114 trial?

5 A. I would assume that being the current
6 trial under way at that time, yes.

7 Q. You go on to state in the same email, "I
8 know we have some definite signs that that is likely
9 not the case," paren, "re early discontinuations,"
10 close parens, "but should we be adjusting
11 assumptions before we really have all the data
12 analyzed," question mark.

13 Do you see that?

14 A. Yes, I do.

15 Q. Now, who -- how did you become aware that
16 there were some definite signs at that point in time
17 that the 114 trial was going to -- well, strike
18 that.

19 What were the definite signs that you
20 refer to in that section?

21 MR. LORENZINI: Objection; lacks foundation.

22 BY THE WITNESS:

23 A. I don't recall, but I -- right here,
24 you -- it says "re early discontinuations."

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1 BY MR. DAVIS:

2 Q. Okay. How did you first learn of the
3 early discontinuations in the 114 trial?

4 A. I don't recall.

5 Q. How did you become aware that the early
6 discontinue -- strike that.7 How did you become aware that the early
8 discontinuations in that trial were a definite sign
9 that something was happening in that trial?10 MR. LORENZINI: Objection; mischaracterizes the
11 document.

12 BY THE WITNESS:

13 A. Yeah, I don't -- I don't understand that
14 question.

15 BY MR. DAVIS:

16 Q. Yeah. What would -- the reference to
17 early discontinuations there, you say that that was
18 a definite sign of something in this email. What
19 was it a definite sign of?

20 MR. LORENZINI: Objection; lacks foundation.

21 BY THE WITNESS:

22 A. I don't -- I don't know what I was
23 meaning there at that time.

24

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1 BY MR. DAVIS:

2 Q. Okay. Was it a definite sign of
3 something having to do with nausea and vomiting?4 A. When I read this, it says "definite
5 sign," "early discontinuations."

6 Q. Do you --

7 A. And I have no recollection of this,
8 so ...9 Q. The whole sentence says, "I also thought
10 that we were assuming the current trial with
11 titration" --

12 A. Um-hmm.

13 Q. -- and we've agreed that's the 114 trial.
14 Correct?

15 A. Yes.

16 Q. It says, "I also thought that we were
17 assuming the current trial with titration" --

18 A. Um-hmm.

19 Q. -- "was supposed to greatly reduce the
20 nausea and vomiting issue," paren, "please let me
21 know if this is a misunderstanding on my part,"
22 close paren. "I know we have --

23 A. Um-hmm.

24 Q. -- "some definite signs that that is

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1 likely not the case," paren, "re early
2 discontinuations," close paren.
3 So the early discontinuations were a
4 definite sign that -- if I -- do I have it correct
5 that the early discontinuations were considered to
6 be a definite sign that the 114 trial was not going
7 to result in a reduction in nausea and vomiting?

8 MR. LORENZINI: Objection; lacks foundation,
9 mischaracterizes the document.

10 BY THE WITNESS:

11 A. I think I can sit here and interpret the
12 sentence just as you are attempting to interpret the
13 sentence. But I can't say that I know what was
14 going through my head at this point in time, so what
15 is there is there.

16 BY MR. DAVIS:

17 Q. Do you have any recollection, as you sit
18 here today, what it was that you were talking about
19 when you said that you had definite signs from the
20 114 trial as of August 2000 that something was
21 likely not the case?

22 MR. LORENZINI: Objection.

23 BY THE WITNESS:

24 A. I -- I'm -- I'm still not following that.

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1 Q. I'm trying to --

2 A. What the definite signs are? As I said,

3 I think the definite signs I would have been

4 referring to here are the early discontinuations.

5 Q. But the early discontinuations are a

6 definite sign of something. Correct?

7 MR. LORENZINI: Objection; vague and ambiguous.

8 BY THE WITNESS:

9 A. Yeah. I -- I don't know.

10 BY MR. DAVIS:

11 Q. So --

12 A. Signs --

13 Q. -- as you sit here today, you can't shed

14 any further light on what it was that you were

15 discussing in this email back in August of 2000.

16 A. No, I have no recollection.

17 Q. Now, where -- where did you get the data,

18 the early discontinuation data that you refer to

19 here?

20 A. I don't recall. But having looked at

21 that prior document -- and I don't know the dates on

22 that prior document -- where you had shown that I

23 was in a meeting where this was discussed, so I

24 would assume that, but I don't recall.

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1 Q. Okay. Do you recall discussions within
2 Abbott regarding any information that could be
3 obtained or gleaned from the early discontinuations
4 that were being experienced in the 114 trial as of
5 August 2000?

6 MR. LORENZINI: Objection to the form of the
7 question.

8 Could you repeat the question?

9 MR. DAVIS: Sure. Could you re-read the
10 question, please?

11 (WHEREUPON, the record was read by
12 the reporter.)

13 MR. LORENZINI: Objection to the form of the
14 question.

15 BY THE WITNESS:

16 A. I would just answer I don't recall any
17 discussions, because I don't ...

18 BY MR. DAVIS:

19 Q. Do you have any recollection of
20 discussions within Abbott regarding data from the
21 114 trial or the potential meaning of any data from
22 the 114 trial before that -- the final results of
23 that trial were unblinded?

24 MR. LORENZINI: Objection; vague and ambiguous.

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1 BY THE WITNESS:

2 A. No. My recollection of the early
3 discontinuation discussions or information would
4 have been we were tracking the progress of the
5 trial.

6 BY MR. DAVIS:

7 Q. Um-hmm.

8 A. I recall us tracking the progress of the
9 trial.

10 Q. And is it fair to say that as of the time
11 that you wrote this email in August of 2000, that
12 you regarded the information regarding -- that you
13 had obtained about the progress of the trial up to
14 that point in time --

15 A. Um-hmm.

16 Q. -- to provide at least some preliminary
17 indication that titration of ABT-594 wasn't going to
18 greatly reduce the nausea and vomiting issue?

19 MR. LORENZINI: Objection; mischaracterizes the
20 witness's prior testimony and vague and ambiguous
21 with respect to the meaning of tracking progress of
22 the trial.

23 THE WITNESS: And after all of that, I -- we
24 need to hear the question again.

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1 MR. DAVIS: Would you actually read my prior
2 question and her answer and then my most recent
3 question, please?

4 (WHEREUPON, the record was read by
5 the reporter.)

6 BY THE WITNESS:

7 A. By the end of that question, I have no
8 idea what you're asking.

9 MR. LORENZINI: That's a pretty confusing
10 question.

11 BY THE WITNESS:

12 A. I have no idea what the question is.

13 BY MR. DAVIS:

14 Q. You mentioned a moment ago that you were
15 tracking the progress of the trial, meaning the 114
16 trial. Right?

17 A. Yes.

18 Q. What did you mean by that? What was
19 Abbott doing in tracking the progress of that trial?

20 A. We do this frequently to track enrollment
21 and number of patients to know are you going to stay
22 on your time line, most -- most typically, is what
23 you're tracking for.

24 Q. Does Abbott track the progress of the

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1 trial for any other reason?

2 MR. LORENZINI: Objection; vague, ambiguous.

3 BY THE WITNESS:

4 A. Yeah. I don't know what Abbott does.

5 BY MR. DAVIS:

6 Q. Based on your observations.

7 A. No.

8 Q. Now, as of August 2000, you were -- you

9 and others within Abbott were tracking the progress

10 of the 114 trial. Is that right?

11 MR. LORENZINI: Objection; mischaracterizes the

12 testimony, vague and ambiguous.

13 BY THE WITNESS:

14 A. Just to be clear, I wasn't doing the

15 tracking. Usually, the clinical group does the

16 tracking. I recall seeing, as we do with many

17 trials, the clinical team puts up a poster actually

18 and adds to it every day, you know, to track the

19 trial.

20 Q. So it --

21 A. I wasn't doing the tracking. So that's

22 why I'm saying --

23 Q. Well, a moment ago you said, "We were

24 tracking the trial."

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1 A. Yes, um-hmm.

2 Q. We -- who was the "we"?

3 A. I'm sorry. "We" -- "we" would have meant
4 Abbott in that case, so the clinical team.

5 Q. So it's okay for me to talk about Abbott
6 tracking the trials. Is that right? You agree that
7 Abbott tracked the progress of the 114 trial.

8 A. If you mean the clinical team on the
9 trial -- trial, yes.

10 Q. And the information that they obtained
11 when tracking the trial was shared with other
12 members of the 594 team, including you?

13 A. Yes, as we've seen.

14 Q. And one of the things that they were
15 tracking were early discontinuations. Is that
16 right?

17 A. Yes.

18 Q. And is it fair to say that, as of August
19 of 2000, you took the early discontinuations to be a
20 definite sign that the 114 trial with titration was
21 not going to greatly reduce the nausea and vomiting
22 issue that was associated with the use of ABT-594?

23 A. Some definite --

24 MR. LORENZINI: Objection.

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1 BY THE WITNESS:

2 A. "Some definite signs" to me, yeah, I was
3 probably being -- I don't know anymore what "some
4 definite signs" mean, but --

5 BY MR. DAVIS:

6 Q. Okay.

7 A. -- I was probably being hyperbole there.

8 Q. Well, can you answer my question --

9 A. I'm sorry.

10 Q. -- which is, did you -- is it fair to say
11 that, as of August 2000, you took the early
12 discontinuations that had been observed in tracking
13 the 114 trial to be a definite sign -- not
14 necessarily the only sign, but a definite sign --
15 that the 114 trial with titration was not going to
16 greatly reduce the nausea and vomiting issue that
17 had been observed with ABT-594?

18 MR. LORENZINI: Objection.

19 BY THE WITNESS:

20 A. In looking at this sentence, it seems
21 that I may have.

22 BY MR. DAVIS:

23 Q. Do you believe you did?

24 MR. LORENZINI: Objection; lacks foundation.

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1 BY THE WITNESS:

2 A. It's odd when you don't remember
3 something to be able to say -- reflect now on it. I
4 don't remember it. I'm interpreting the sentence.

5 BY MR. DAVIS:

6 Q. But looking at it today, that's what you
7 think you meant. Right?

8 MR. LORENZINI: Objection.

9 You can answer.

10 BY THE WITNESS:

11 A. Yeah, I guess.

12 BY MR. DAVIS:

13 Q. Do you recall any other discussions
14 within Abbott about tracking the progress of the
15 ABT-594 trial?

16 A. No.

17 Q. Do you recall any -- receiving any
18 feedback from Dr. McCarthy or anyone else working on
19 the 114 clinical trial concerning the statements
20 that you made in this particular email that has been
21 marked as Exhibit 6?

22 MR. LORENZINI: Objection; vague and ambiguous.

23 BY THE WITNESS:

24 A. Yeah, I'm sorry. Do I remember receiving

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1 MR. LORENZINI: I object to your
2 characterization of my asking the question to be
3 re-read.

4 MR. DAVIS: Would you re-read the question,
5 please, so that we can get on with this?

6 (WHEREUPON, the record was read by
7 the reporter.)

8 BY MR. DAVIS:

9 Q. What do you recall, Ms. Landsberg?

10 MR. LORENZINI: Objection.

11 But you can answer.

12 BY THE WITNESS:

13 A. What I was going to say was I recall,
14 even when I left this compound, that we were hopeful
15 that we would continue development. That's what I
16 recall. So I can't believe I had ever recalled
17 anything -- or I had ever thought anything
18 differently.

19 BY MR. DAVIS:

20 Q. You never thought that the preliminary
21 data that had been received on the 114 trial made it
22 less likely that Abbott would continue development
23 of ABT-594?

24 MR. LORENZINI: Objection; asked and answered.

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1 BY THE WITNESS:

2 A. Yeah, no.

3 MR. DAVIS: Let's mark this as the next
4 exhibit, please.5 (WHEREUPON, a certain document was
6 marked Landsberg Deposition Exhibit
7 No. 8, for identification, as of
8 2/16/07.)

9 BY MR. DAVIS:

10 Q. Ms. Landsberg, you have what's been
11 marked as Exhibit 8. Would you look at this
12 document for a moment and tell me if you've ever
13 seen it before?

14 A. No, I don't recall seeing it before.

15 Q. As you sit here today, do you have any
16 doubt that you sent this email, the top email that's
17 dated September 27th, 2000?18 A. No, no reason to believe that I didn't
19 send it.

20 Q. Who is Bob Weiland?

21 A. Bob Weiland, he was -- I don't remember
22 what his title was. I know he was someone who had
23 been at Abbott prior to my arrival there. He's no
24 longer there.

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1 commercial business unit that marketed Depakote.

2 Q. Is Depakote a different compound from
3 ABT-594?

4 A. Yes.

5 Q. What responsibilities did Mr. Marasco
6 have with respect to ABT-594?

7 A. No direct responsibilities.

8 Q. What was the purpose of this meeting
9 that's referenced in Exhibit 9?

10 A. I don't recall.

11 MR. DAVIS: Let's mark this, please, as the
12 next exhibit, Exhibit 10.

13 (WHEREUPON, a certain document was
14 marked Landsberg Deposition Exhibit
15 No. 10, for identification, as of
16 2/16/07.)

17 BY MR. DAVIS:

18 Q. Ms. Landsberg, you have what's been
19 marked as Exhibit 10 at your deposition.

20 A. Um-hmm.

21 Q. Would you please take a moment, read this
22 document to yourself, and then tell me when you're
23 done, please?

24 A. Okay.

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1 Q. This appears to be an exchange of emails
2 that you had with Dr. McCarthy, among others, at
3 Abbott in October of 2000.

4 Do you see that?

5 A. Yes, I do.

6 Q. Did you write the email that's at the
7 bottom of Exhibit 10?

8 A. I have no reason to believe I didn't.

9 Q. It's an email from you to Mr. Weiland,
10 among others. Do you see that?

11 A. Yes, I do.

12 Q. And it references -- it says, "Bob, as
13 you, Rose, and I had discussed, if we move forward
14 to set up a presentation of information to Purdue,
15 the following people could probably do the
16 presenting on key topics."

17 Do you see that?

18 A. Yes, I do.

19 Q. And there's a reference there to
20 "Preclinical ABT-594: Jim Sullivan."

21 A. Um-hmm.

22 Q. "Clinical ABT-594: Bruce McCarthy."

23 A. Um-hmm.

24 Q. "Preclinical and clinical plan ABT-963:

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1 **George Carter."**

2 A. Um-hmm.

3 Q. "Market opportunity/business rationale:

4 **Andrea Landsberg."**

5 Do you see that?

6 A. Yes, I do.

7 Q. Does this refresh your recollection on

8 whether there were any discussions between Abbott

9 and Purdue regarding ABT-594?

10 A. I still don't recall the meeting,

11 although I have no reason to doubt that this is

12 true.

13 Q. Well, do you recall that Abbott had

14 communications with Purdue in this time frame

15 regarding ABT-594?

16 MR. LORENZINI: Objection; asked and answered.

17 BY THE WITNESS:

18 A. No, I don't recall.

19 BY MR. DAVIS:

20 Q. You don't recall ever making any

21 presentation to Purdue regarding market

22 opportunities or business rationale for ABT-594?

23 A. No, I don't.

24 Q. Do you recall sending this email to

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1 MR. ELSEY: And we are back on the video record
2 at 1:17 p.m. This is tape 3.

3 MR. DAVIS: Would you please mark this as the
4 next exhibit? We're up to No. 11.

5 (WHEREUPON, a certain document was
6 marked Landsberg Deposition Exhibit
7 No. 11, for identification, as of
8 2/16/07.

9 ANDREA LANDSBERG,
10 re-called as a witness herein, having been
11 previously duly sworn, was further examined and
12 testified as follows:

13 EXAMINATION (Continued)
14 BY MR. DAVIS:

15 Q. Welcome back, by the way. Ms. Landsberg,
16 you have what's been marked as Exhibit No. 11.
17 Would you look at this document for a moment and
18 please tell me if you've ever seen it before?

19 A. Not outside the context of preparing for
20 today. I don't remember it outside of the context
21 of preparing for today.

22 Q. All right. The first page appears to be
23 an email from you to Chris Silber and to
24 Ms. Waleska. Do I have that right?

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1 A. Yes.

2 Q. And this is for a -- some sort of

3 presentation to Dr. Jeffrey Leiden. Is that right?

4 A. Yes, it appears to be.

5 Q. What presentation is that?

6 A. I don't recall.

7 Q. Did you -- do you recall participating at

8 any point in time in any presentation to Dr. Leiden

9 regarding 594?

10 A. No.

11 Q. Did you prepare the slides that are

12 attached to Exhibit 11?

13 A. I don't recall preparing them.

14 Q. Do you believe that you prepared them?

15 A. I have no reason to doubt, looking at

16 this that I prepared them.

17 Q. Would you look, please, at the page of

18 the slides with the Bates number that ends in 6823

19 in the lower right-hand corner?

20 A. Yes.

21 Q. The slide there says, "ABT-594: Current

22 v DDC Profile."

23 Do you see that?

24 A. Yes.

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1 that's what you intended when you wrote this?

2 A. It's obviously what we -- yes, it's what

3 we thought was the profile as of 9/00.

4 Q. Would you turn, please, to the page that

5 ends in Bates number 6832? There's a slide there

6 titled "Key Product Challenges."

7 Do you see that?

8 A. Yes, I do.

9 Q. And by "key product challenges," is it

10 fair to say you meant to -- you're seeking to

11 identify particular problems that ABT-594 faced in

12 order to be commercialized successfully?

13 MR. LORENZINI: Objection; vague and ambiguous.

14 BY THE WITNESS:

15 A. I think it says just what it says. It's

16 key product challenges.

17 BY MR. DAVIS:

18 Q. What does that mean?

19 A. Challenges that we know potentially the

20 product will have and that we need to be aware of.

21 Q. Challenges to do what? Or challenges

22 before what can be achieved?

23 MR. LORENZINI: Objection; assumes facts not in

24 evidence.

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1 BY THE WITNESS:

2 A. Challenges to do what? I mean, we tend
3 to just have opportunities and challenges. You kind
4 of show both sides of the picture in whatever we do.
5 If I would flip back, I'm almost thinking the prior
6 slide might be opportunities. So it's -- it's very
7 common for us to show both for any product.

8 BY MR. DAVIS:

9 Q. The key product challenges, are these
10 challenges that ABT-594 faced in -- before it could
11 be commercialized?

12 A. Before it can be commercialized? No,
13 because you often market products -- and, again, I'm
14 not speaking specifically here, because I'm not
15 remembering this. But in general, your products,
16 whether they're on the market or not, have benefits
17 and challenges that you are always facing.

18 So I don't believe that that reflects to
19 commercialize. I mean, even on-market products have
20 challenges that you're always identifying --

21 Q. What --

22 A. -- as a marketer. So I don't think it
23 has anything to do with being on-market or the
24 phrase you used there.

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1 Q. My question, though, is: How did these
2 particular items that are identified on the slide
3 present challenges to ABT-594?
4 A. It would have been challenges that, from
5 a marketing perspective, you would have to know that
6 you might have to deal with in how you approached
7 selling the product.

8 Q. Okay.

9 A. I mean, that's very clearly laid out
10 under "Nicotinic mechanism, will require pre-launch
11 market education and priming to diffuse negative
12 association." So it's talking about -- this whole
13 page is saying when we go to market, these are
14 things that a marketing person would need to know to
15 appropriately position and market the product.

16 Q. The first bullet point is titled
17 "Tolerability," and the subpoint says, "Competition
18 has clear advantage on tolerability."

19 How was it that the competition had a
20 clear advantage on tolerability over ABT-594 at the
21 time that these slides were prepared?

22 MR. LORENZINI: Objection.

23 BY THE WITNESS:

24 A. Yeah. Me not remembering why I wrote

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1 this or which -- and not looking at the prior slides
2 here to get a sense of where this falls in the
3 stack, I don't know which competition I might be
4 referring to here.

5 BY MR. DAVIS:

6 Q. As you sit here today, do you have any
7 recollection as to why it was that, on this slide,
8 you wrote, "The competition has clear advantage on
9 tolerability"?

10 A. I could speculate it was because of
11 Neurontin's known very clean tolerability. It
12 was -- we called it placebo, because it basically
13 had very little efficacy and very little side
14 effects.

15 Q. Were there any particular adverse events
16 or side effects that associated with ABT-594 that
17 you thought were -- presented a disadvantage with
18 respect to the competition?

19 MR. LORENZINI: Objection; vague, ambiguous,
20 misleading.

21 BY THE WITNESS:

22 A. Could you rephrase that or say it again?

23 BY MR. DAVIS:

24 Q. Well, it says here that "Competition has

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1 Here's -- here's what I can answer and what I can
2 say is that you always look at your compounds, any
3 compound that you have, and are looking at what that
4 compound has versus other compounds, working towards
5 making improvements. You make improvements in your
6 current products.

7 BY MR. DAVIS:

8 Q. Um-hmm.

9 A. So improvements required for back-up, no.

10 Q. My --

11 A. This is -- this must reflect exactly what
12 we were seeing in 594.

13 Q. Um-hmm.

14 A. This is my assumption.

15 Q. Um-hmm. Do you recall any discussions
16 within Abbott on any of the topics identified on
17 that slide?

18 A. I do not recall discussions on those.

19 MR. DAVIS: Let's mark this as the next
20 exhibit, please.

21 (WHEREUPON, a certain document was
22 marked Landsberg Deposition Exhibit
23 No. 18, for identification, as of
24 2/16/07.)

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1 THE WITNESS: Can I say --

2 MR. LORENZINI: -- to the question phrased that

3 way.

4 THE WITNESS: So I just say no --

5 MR. LORENZINI: No, excluding our --

6 THE WITNESS: -- excluding --

7 MR. LORENZINI: Excluding our meeting

8 yesterday.

9 BY THE WITNESS:

10 A. No, excluding our meeting yesterday.

11 BY MR. DAVIS:

12 Q. Okay. That's fine.

13 Why don't we give her a moment to look at

14 this one?

15 A. Okay. I didn't look the attachment, if

16 you want me to do that, too.

17 Q. Please take a moment to look at the

18 attachment.

19 A. Okay.

20 Q. All right. Do you recall any of the

21 email communications that are -- have been marked as

22 Exhibit 18?

23 A. No.

24 Q. The first email communication, I think,

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1 in time that's listed here appears to be yours,
2 dated November 29th, 2000, at 7:17 a.m., to a Larry
3 Lin, Dr. Silber, and others.

4 Do you see that?

5 A. Yes, I do.

6 Q. Who is Larry Lin?

7 A. I've been seeing his name on a lot of
8 things, and I'm still trying to place him. I'm
9 having difficulty remembering him.

10 Q. Your email --

11 A. So I --

12 Q. I'm sorry.

13 A. I don't know. I just can't remember.

14 Q. Your email under the subject says
15 "ABT-594 Forecast Scenarios for BD Partnering."

16 What is BD partnering?

17 A. Business development.

18 Q. What -- what do you recall that -- what,
19 if any, activities or communications do you recall
20 concerning business development partnering for
21 ABT-594?

22 A. I don't recall prior to seeing this. I
23 don't recall now.

24 Q. Attached to your email are some slides

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1 for ABT-forecast potential. Do you see that?

2 A. Yes, I do.

3 Q. Where did you obtain the information
4 contained in these slides?

5 A. I probably would have been the one to
6 develop these sales forecasts.

7 Q. Did you think that they were reasonable
8 forecasts at the time they were developed?

9 A. Yes.

10 Q. And the -- your email to Mr. Lin, among
11 others, it says at the bottom, "Larry, please let me
12 know if these numbers look acceptable. Some of them
13 may already be optimistic. BD's call as to whether
14 you want to inflate them for best case scenario."

15 What did you mean by that?

16 A. Business development might have wanted to
17 take a different look at it and increase the upside.

18 Q. And it looks like Mr. Weiland responded
19 to your email later in the day on November 29th.

20 Do you see that?

21 A. Yes, do I.

22 Q. He says, "Andrea, this looks like a
23 decent starting point. OxyContin will do over
24 1 billion by itself. I'm wondering if our upsides

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1 don't take us well over the \$1 billion mark."

2 Do you see that?

3 A. Yes, I do.

4 Q. At the time that these emails were

5 prepared in late 2000, did you think that ABT-594

6 had the potential to be a \$1 billion drug?

7 MR. LORENZINI: Objection to the form of the

8 question.

9 BY THE WITNESS:

10 A. I can only look to what are the forecasts

11 here and say that with the development plan, it

12 looks like I did.

13 BY MR. DAVIS:

14 Q. And, again, I take it at the time that

15 you were preparing these, you were trying to be as

16 accurate as you could. Correct?

17 A. Absolutely. These are fairly precise

18 numbers.

19 MR. DAVIS: Let's mark this, please, as the

20 next exhibit. We're up to 19.

21 (WHEREUPON, a certain document was

22 marked Landsberg Deposition Exhibit

23 No. 19, for identification, as of

24 2/16/07.)

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1 BY MR. DAVIS:

2 Q. Would you read this document to yourself,

3 Ms. Landsberg, and please tell me when you're done?

4 A. Okay.

5 Q. Now, this appears to be an email from a

6 Jennifer Dart to you, among others, at Abbott.

7 Do you see that?

8 A. Yes.

9 Q. Who is Jennifer Dart?

10 A. I remember a Jenny Dart and can picture

11 her. I'm not remembering which group she worked

12 with. It looks -- yeah, I don't know.

13 Q. As you --

14 A. DSG maybe.

15 Q. I'm sorry.

16 A. DSG maybe.

17 Q. As you sit here today, Ms. Landsberg, do

18 you have reason to believe that you did not receive

19 this email in or about December of 2000?

20 A. No, I do not.

21 Q. The email subject is "Analgesia Internal

22 Review Notes." And the first line says, "Thanks to

23 everyone for your participation in the analgesia

24 internal review."

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1 What was that?

2 A. I don't recall.

3 Q. It goes on to state, "Andrea, Laura, or

4 Chris, will one of you please set up some time with

5 Rock to review the project assumptions and

6 forecasts?"

7 What does that refer to?

8 A. What does which part of it refer to?

9 Q. Well, it says -- any of it. It says,

10 "Will you please set up some time with Rock to

11 review the project assumptions and forecasts."

12 What project assumptions and forecasts

13 are referred to there?

14 A. I don't recall what this was, so I don't

15 know which project she's referring to.

16 Q. Further on down in the same email, it

17 says, "Following is the list of follow-up items from

18 the meeting. ABT-594, Andrea will reduce forecast

19 to reflect vomiting AE."

20 Do you see that?

21 A. Yes, I do.

22 Q. Why was it that you were reducing

23 forecasts at that point in time to reflect vomiting

24 adverse offense -- events associated with ABT-594?

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1 MR. LORENZINI: Objection to the form of the
2 question.

3 BY THE WITNESS:

4 A. I don't recall.

5 BY MR. DAVIS:

6 Q. Do you recall, in fact, reducing some
7 forecasts associated with ABT-594 to reflect adverse
8 events of vomiting?

9 A. No, I don't recall that.

10 Q. Do you have any recollection of what
11 forecasts are referred to in this email?

12 A. The forecast is the forecast. I don't
13 know what that would mean, what forecasts? The 594
14 forecast, the 089 forecast, the Hydrocodone
15 forecast.

16 Q. Well, this one is under ABT-594. Do you
17 see that?

18 A. Yes.

19 Q. Okay. So is that --

20 A. So it looks like it would be the ABT-594
21 forecast.

22 Q. Is that the sales forecast?

23 A. You don't distinguish the sales or the --
24 you know, the product. Sometimes you show your

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1 forecast in sales. Sometimes you show your forecast

2 in units --

3 Q. Um-hmm.

4 A. -- volume, you know. Product -- number

5 of pills. So forecast could mean either one of

6 those.

7 Q. As -- as you sit here today, do you have

8 any recollection of ever adjusting your forecast for

9 ABT-594 to reflect adverse events of vomiting?

10 A. Not -- no.

11 Q. Do you have a --

12 A. I recall we -- we always -- you always

13 adjusted your forecasts over time. That was our

14 job.

15 Q. Um-hmm. My question is a little bit

16 different.

17 A. I know.

18 Q. My question is --

19 A. That's why I'm saying I don't recall

20 that -- that -- I don't recall that.

21 Q. Do you recall why it was necessary at any

22 point in time to adjust your forecast to reflect

23 adverse events involving vomiting?

24 MR. LORENZINI: Objection to the form of the

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1 question.

2 BY THE WITNESS:

3 A. Why it would be necessary?

4 BY MR. DAVIS:

5 Q. Um-hmm.

6 A. If you had -- you know, just like
7 anything, any time you have information -- no, I
8 don't understand why necessary.

9 Q. I'm sorry?

10 A. I'm -- I'm not understanding the way that
11 question is phrased.12 Q. Well, it appears from this email that you
13 were going to reduce some forecast information
14 associated with ABT-594 --

15 A. Yes.

16 Q. -- to reflect vomiting adverse events.

17 A. Um-hmm.

18 Q. And my question is, you don't -- do you
19 have any recollection as to why that was so or why
20 you were going to do that in that time frame?21 A. No, I don't even remember this happening,
22 this meeting.23 MR. DAVIS: Let's mark this, please, as the
24 next exhibit.

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1 BY MR. DAVIS:

2 Q. Would you turn, please, to the fourth
3 page of the presentation, the one that's numbered in
4 the lower right-hand corner 2925?

5 A. Yes.

6 Q. Do you see Abbott's "Internal R&D
7 Challenges"?

8 A. Yes.

9 Q. And do you see that there's a reference
10 there to a series of compounds, one of which is
11 ABT-594?

12 A. Yes.

13 Q. And if you look at the -- the key in the
14 lower right-hand corner, it appears that ABT-594 is
15 in green print, which correlates to "Questionable
16 viability" under "Commercial Potential."

17 Do you see that?

18 A. Yes, I do.

19 Q. Were you aware in late 2000 that
20 Dr. Leiden had made a presentation that listed
21 ABT-594 as having questionable commercial potential
22 or questionable viability with respect to its
23 commercial potential?

24 A. No, I was not.

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1 Q. Did you ever hear anything, any
2 discussion within Abbott about such a presentation
3 by Dr. Leiden?

4 A. He was making a lot of presentations to
5 the R&D organization that I was aware of about their
6 structure and things he was going to change. That I
7 was very aware of because we knew that. That was a
8 big thing. He was going to reorganize R&D.

9 Q. Did you ever hear or learn at any point
10 in time in, say, late 2000 or early 2001 --

11 A. Um-hmm.

12 Q. -- that Dr. Leiden had stated or made a
13 presentation in which he indicated that ABT-594 was
14 regarded as having questionable viability or
15 questionable commercial potential?

16 A. No.

17 MR. DAVIS: Let's mark this as the next
18 exhibit, please. I'm sorry. I'm sorry. We're up
19 to Exhibit 21.

20 (WHEREUPON, a certain document was
21 marked Landsberg Deposition Exhibit
22 No. 21, for identification, as of
23 2/16/07.)

24

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1 read that to yourself and then tell me when you're
2 done, please.

3 A. Okay.

4 Q. Does this document refresh your
5 recollection in any way about preparing any slides
6 for a presentation for Dr. Leiden in late January or
7 so of 2001?

8 A. No.

9 MR. DAVIS: Let's mark this as the next
10 exhibit, please, 26.

11 (WHEREUPON, a certain document was
12 marked Landsberg Deposition Exhibit
13 No. 26, for identification, as of
14 2/16/07.)

15 BY MR. DAVIS:

16 Q. Ms. Landsberg, you have what has been
17 marked as Exhibit 26. Would you look at this
18 document for a moment --

19 A. Um-hmm.

20 Q. -- and tell me if you recognize it?

21 A. No.

22 Q. It appears in the first page to be an
23 email from you to Tom Woidat, with a cc to Michael
24 Biarnesen, regarding "financial slides for Leiden

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1 meeting, 2/2."

2 Do you see that?

3 A. I do.

4 Q. Did you prepare the slides that are
5 attached?

6 A. I have no reason to believe I did not.

7 Q. Do you recall doing so?

8 A. No.

9 Q. The first slide deals with ABT-594 global
10 forecast ranges.

11 Do you see that?

12 A. Yes.

13 Q. Where did you get global forecast data
14 for ABT-594?

15 A. I'm assuming the global refers to the
16 fact that there's US and Ex-US down below.

17 Q. Um-hmm.

18 A. So the US ones -- the US ones would have
19 been developed by me at this point in time, it
20 seems, and the Ex-US, I think it was still Laura.

21 So ...

22 Q. By the way, in developing that forecast
23 data, did you have assistance from others in Abbott?
24 A. If by "assistance from others" you mean

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1 A. The numbers?

2 Q. The forecast that we see here, lots of
3 people within Abbott would provide information that
4 would be utilized for purposes of coming up with
5 these forecasts. Is that right?

6 A. I -- I don't know.

7 MR. LORENZINI: Objection.

8 BY THE WITNESS:

9 A. I don't -- I think "lots" is the wrong
10 word. I think there's a few groups that you might
11 have to go to for those different pieces of
12 information.

13 BY MR. DAVIS:

14 Q. Okay. Did you go to all of the groups
15 that you thought were necessary to come up with the
16 forecast data?

17 A. I don't recall specifically who I went to
18 in this case.

19 Q. Um-hmm.

20 A. I would assume that I would, because we
21 were striving to be accurate.

22 Q. Were these numbers, to the best of your
23 knowledge, accurate as of the time that these slides
24 were prepared?

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1 A. I would have to believe I -- I thought

2 so, yes.

3 Q. The -- the next slide simply adds

4 additional information regarding NPV. Is that
5 right?

6 A. Yes.

7 Q. "NPV" being net present value?

8 A. Correct.

9 Q. And how did you go about calculating that
10 at that time?

11 A. I don't recall how we calculated it at
12 that point in time, quite honestly.

13 What I would imagine I did is what I
14 would do now. Well, no. What I would do now is I
15 would ask someone in finance to do it for me.

16 But you can just go into a spreadsheet,
17 and there's usually a function that you highlight
18 the -- you know, the cells, your -- your cash
19 stream, your margin stream, in this case it would
20 be, and click the button that calculates it.

21 You get your discount rate. Usually, we
22 always have a -- whatever the current discount rate
23 is that Abbott is using to discount any of its cash
24 flows for NPVs. That's something that you usually

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1 BY MR. DAVIS:

2 Q. Ms. Landsberg, you have what's been
3 marked as Exhibit 28 for your deposition. Would you
4 look at this document for a moment and tell me if
5 you can identify it for me?

6 A. If I can identify it for you?

7 Q. Yes.

8 MR. LORENZINI: Other than what's on the title
9 page?

10 BY MR. DAVIS:

11 Q. Yes. Do you -- do you recognize it?

12 A. Not outside preparation for this meeting.

13 Q. I'm sorry?

14 A. And even then I'm not sure.

15 Q. Would you look, please, at the pages
16 that -- Bates stamped in the lower right-hand corner
17 ends in 2435, please?

18 A. 2435?

19 Q. Yes.

20 A. Yes.

21 Q. Okay. Do you see that there's a titled
22 slide there that says "ABT-594 Project Review"?

23 A. Yes.

24 Q. "February 2, 2001, Commercial Assessment

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1 Andrea Landsberg, Laura Robinson."

2 Do you see that?

3 A. Yes, I do.

4 Q. Do you recall making any joint

5 presentations with Ms. Robinson on ABT-594?

6 A. No.

7 Q. If you'd look, please, at the slides in

8 this section of the presentation, the commercial

9 assessment section, are those slides that you

10 prepared or helped to prepare?

11 A. I don't recall preparing them. I have no

12 reason to doubt that I might have. It looks like my

13 name on it.

14 Q. Would you take a look at the slide that

15 Bates number ends in 2445?

16 A. Qualitative Market Research?

17 Q. Yes.

18 A. Yes.

19 Q. What do we see in this slide?

20 A. This appears to be showing what we tested

21 and some qualitative market research as far as a

22 product profile. And it's --

23 Q. What's the --

24 A. It's in --

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1 Q. I'm sorry.

2 A. I was just going to say perhaps about

3 594, since that's the preceding slides.

4 Q. What was the qualitative market research

5 that Abbott performed concerning ABT-594?

6 A. I don't recall.

7 Q. All right. Was it done by someone within

8 Abbott? Or was it done by someone outside of

9 Abbott?

10 A. I'd say it's almost 100 percent sure to

11 have been done by someone outside of Abbott, because

12 we always contract with a third party to do our

13 market research.

14 Q. Um-hmm.

15 A. It's -- you never do your own market

16 research. You always work with a market research

17 firm.

18 Q. What market research firms were you

19 working with in the 2000 --

20 A. I --

21 Q. -- 2001 time frame?

22 A. I have no recollection.

23 Q. Was their -- is the information provided

24 to you by the market research firm provided to you

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1 A. Um-hmm.

2 Q. -- there's a reference to "Equivalent,"

3 "Equivalent," and then "Poor."

4 Do you see that?

5 A. Um-hmm.

6 Q. What does that mean?

7 A. Typically, in this type of research, you

8 know, before a product -- before you know what a

9 product's going to look like, you test various

10 profiles.

11 So this is saying, you know, one profile

12 is probably efficacy better than current,

13 equivalent, AEs, efficacy same, equivalent AEs,

14 efficacy better, poorer versus -- AEs versus current

15 agents. It looks like it's three profiles that were

16 tested in the market research.

17 Q. Would you look, please, at the page

18 that's numbered Bates stamp ends in 2452? It's

19 titled "Key Product Challenges."

20 A. Um-hmm.

21 Q. It says, "Key challenge is achieving

22 optimal balance of tolerability and efficacy to

23 satisfy both US and Ex-US markets."

24 Do you see that?

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1 low side effect -- certainly compared to those
2 others that were available -- so having an
3 advantage.

4 Q. The next sub-bullet point says, "Will
5 need to minimize early DCs as much as possible."

6 What are DCs?

7 A. Probably standing for discontinuation.

8 Q. What do you -- what did you mean when you
9 said "Will need to minimize early discontinuations
10 as much as possible"?

11 A. If you're launching a product and you
12 have physicians using a product -- a new product for
13 the first time, especially one in a new class, but
14 now, in this day and age, any new product coming
15 out, their first experience with it is very
16 critical.

17 And you want to make sure you're, you
18 know, giving guidance to physicians on selecting the
19 right type of patient, using the right dosing,
20 et cetera, so that they don't experience and get a
21 negative reaction on the first patients that they
22 use it.

23 Q. And why did that present a particular
24 challenge for ABT-594?

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1 A. I think it presents a problem for any
2 product coming on the market.

3 Q. So these are key product challenges, not
4 for ABT-594, but for any product entering the
5 market. Is that your testimony?

6 MR. LORENZINI: Objection; argumentative.

7 BY THE WITNESS:

8 A. No, I guess here they are. You need to
9 minimize dis- -- early discontinuations in this
10 case. That's probably what we thought.

11 BY MR. DAVIS:

12 Q. Why did you think that that was a
13 particular challenge --

14 A. Because we --

15 Q. -- a key product challenge for ABT-594?

16 A. Because we knew the product had early AEs
17 in all the other clinical trials.

18 Q. Now, would you turn the page that's Bates
19 numbered 24 -- it looks like 56, "ABT-594 Go/No-Go
20 Process." Do you see that?

21 A. Yes.

22 Q. And it says, "What will a Go decision
23 look like? Patients and physicians will have
24 compelling reasons to choose ABT-594 versus other

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1 MR. DAVIS: Why don't we take a few minutes,
2 and I'll see if there's anything else I want to ask.

3 MR. LORENZINI: Okay.

4 MR. ELSEY: All right. Going off the video
5 record at 3:15 p.m.

6 (WHEREUPON, a recess was had from
7 3:15 p.m. until 3:19 p.m.)

8 MR. ELSEY: And we are back on the video record
9 at 3:19 p.m.

10 BY MR. DAVIS:

11 Q. Ms. Landsberg, what information from the
12 114 study did you see while that study was still --
13 still under way?

14 A. I'm trying to remember if I saw any
15 information. I know we were tracking the
16 enrollment and, from what I've seen here, the
17 drop-out rates. But that's what I recall. I
18 wouldn't have recalled even that.

19 Q. Do you recall seeing any information on
20 adverse events?

21 A. Not prior to yesterday, in preparation of
22 this meeting.

23 Q. I think you mentioned earlier today that
24 you remember the -- there was information presented

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1 about the clinical trial --

2 A. Um-hmm.

3 Q. -- while it was under way and that there

4 would be -- at various meetings, there would be

5 information added to what previously had been

6 presented. Do you recall that?

7 A. No, I'm not following what you're saying.

8 On that particular trial? Or just about the

9 product?

10 Q. Well, do you recall at any point in

11 time --

12 A. Um-hmm.

13 Q. -- seeing anyone and -- make any

14 presentations or providing any information regarding

15 the 114 trial while that trial was under way?

16 A. I don't remember much specifically at --

17 I don't remember any -- much of anything from this

18 point in time at this job at this point. So, no, I

19 do not remember that.

20 Q. So the only data that you recall

21 receiving in the course of the trial was information

22 about enrollment and drop-out rates.

23 A. And if it hadn't been for what I've seen

24 here, I think I probably would have just remembered

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1 that chart on the wall tracking the patients.

2 Q. What is that chart on the wall that you
3 recall?

4 A. It was -- it was a -- you know, a chart
5 that had the time line and patients. And they would
6 update it kind of every day on how many patients
7 were in the trial.

8 Q. I --

9 A. That I can specifically remember, because
10 I -- I used to walk by it.

11 Q. Where -- where did you walk by it?

12 A. That was over in the -- the venture area.
13 I think it was like right outside of Chris Silber's
14 office, and there was a conference room there.
15 So -- Mike was there. I mean, they were all there,
16 so -- "they" meaning, you know, Mike and -- and
17 Bruce and Chris, where their offices were.

18 Q. How big was the chart?

19 A. Oh, I don't know. I don't think it was
20 very big. It was like a poster size -- you know, a
21 poster board, a poster size, like that, if you can
22 estimate that, four-by-three or something
23 (indicating).

24 Q. And you recall the chart was updated

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1 periodically?

2 A. Yes.

3 Q. Who was updating the chart?

4 A. I wouldn't have been able to say. I'm

5 wondering if it was Marilyn Collicott or -- I

6 just -- I think she -- it seems like she was the

7 CRA, and that would be who would normally be

8 updating those chart.

9 Q. What color was the chart?

10 A. I haven't the faintest. That I don't
11 remember.

12 Q. Do you recall what the chart was titled?

13 A. No.

14 Q. And was it the same chart that someone
15 was manually updating, or was it a new printout of a
16 chart?

17 A. I don't remember that, either.

18 Q. What kind of material was the chart on?

19 A. I think it was paper or I think it was
20 like a poster board.

21 Q. What ultimately happened to the chart?

22 A. I haven't the faintest idea.

23 Q. And you said it was in the venture office
24 or the venture area?

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1 A. Venture area.

2 Q. What was the venture area?

3 A. As I was saying, just where Chris

4 Silber's offices were there, those people who were

5 in that venture were sitting.

6 Q. Was that where Dr. McCarthy's office was

7 located --

8 A. Yes.

9 Q. -- as best recall?

10 Can you identify any other people who you

11 remember having offices in that area?

12 A. Mike Biarnesen. Those are the three

13 offices I remember right there in that area.

14 Q. Approximately over what period of time do

15 you recall seeing that chart?

16 A. I -- I don't know.

17 Q. It was while you were working on ABT-594?

18 A. Yes. That's the only time I would have

19 been over in that building. I don't even remember

20 which building it was. I think it was AP 34.

21 Q. Did you periodically check the chart

22 yourself?

23 A. I didn't go over there to check it. I

24 would look at it, obviously, when I walked by it,

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1 know, other than seeing what I'm seeing here. And,
2 no, I left this product still hoping we would launch
3 this product.

4 Q. My question, I think, is a little bit
5 different, though.

6 A. Um-hmm.

7 Q. My question is: While you were working
8 on this product, do you recall receiving any
9 information about the 114 study that caused you to
10 be concerned about the commercial viability of
11 ABT-594?

12 MR. LORENZINI: Objection.

13 BY THE WITNESS:

14 A. No. No. I'm going to say no, even based
15 on the fact of what I saw even in February, what
16 I -- I still thought it was commercially viable.

17 BY MR. DAVIS:

18 Q. But it didn't cause you to have any
19 greater concerns at any point in time about the
20 commercial viability of ABT-594.

21 MR. LORENZINI: Objection; vague and ambiguous.

22 BY THE WITNESS:

23 A. Yeah. I think you're concerned about
24 everything you're hearing about a product.

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1 Q. -- having any concerns or heightened
2 concerns about the commercial viability of ABT-594?

3 A. No, I do not recall.

4 Q. And I -- are you aware of any significant
5 changes in the development or the developmental
6 strategy for ABT-594 that were made in the late
7 2000/early 2001 frame?

8 MR. LORENZINI: Objection; vague.

9 BY THE WITNESS:

10 A. I would say no, I'm not aware of any
11 major changes.

12 BY MR. DAVIS:

13 Q. Who decided to terminate the development
14 of ABT-594, if you know?

15 A. I don't know.

16 Q. Why did they decide to term- -- why did
17 they decide to terminate the development of ABT-594?

18 MR. LORENZINI: Objection; lacks foundation.

19 BY THE WITNESS:

20 A. I don't know. I'm assuming the Phase IIb
21 trial did not hit; i.e., it wasn't efficacious.

22 BY MR. DAVIS:

23 Q. Are you aware of any -- aware of any
24 efforts by Abbott to out-license ABT-594?

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1 A. No. I've seen it in the documents you've
2 shown me, but, no, I don't recall that.

3 Q. Are you aware of any efforts by Abbott in
4 the summer or fall of 2000 to recruit or to hire a
5 patient recruitment firm for purposes of the 114
6 trial?

7 A. No, I'm not, although that's a common
8 practice --

9 Q. How do you --

10 A. -- in clinical trials.

11 Q. I mean, how do you --

12 A. I mean patient recruitment.

13 Q. How do you know that it's a --

14 A. We --

15 Q. -- common practice for Abbott to retain
16 patient recruitment firms?

17 A. Because in my discussions with clinical
18 people and when we had other trials going on, I've
19 been told that, yes, this is something that you can
20 do to speed up your trial.

21 Q. How --

22 A. You recruit more patients into your
23 trial. And I've been involved since this in -- not
24 phase -- not earlier phase work, but Phase IV

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1 trials.

2 Q. That you've actually used a patient
3 recruitment firm?

4 A. I know we've talked -- we talked about it
5 on one trial. I don't know whether we ended up
6 using it. We used advertising, I know, recruited
7 through -- we put fliers out near the sites to
8 recruit patients that way.

9 Q. Have you ever worked on a compound at --
10 at Abbott in which a -- Abbott has actually retained
11 a patient recruitment firm to assist in clinical
12 trials?

13 A. No, I don't remember.

14 MR. DAVIS: I have no further questions at this
15 time.

16 MR. LORENZINI: I have no questions.

17 MR. DAVIS: We're done.

18 MR. ELSEY: Okay. Going off the video record
19 at 3:29 p.m.

20 MR. LORENZINI: Signature reserved.

21 AND FURTHER DEPONENT SAITH NOT

22

23

24

Landsberg Deposition Exhibit 4

P's Exhibit SL

Andrea
Landsberg /LAKE/PPD/ABBO
TT
08/07/2000 05:54 PM

To Bruce McCarthy/LAKE/PPRD/ABBOTT@ABBOTT
cc Christopher J Silber/LAKE/PPRD/ABBOTT@ABBOTT,
Michael K Barnesen/LAKE/PPRD/ABBOTT@ABBOTT
bcc
Subject 594 development plan

Bruce,

I am forwarding this latest version to you as I was planning on having it all done today but got sidetracked helping Rose with a fire drill for Arthur for 4 hours this afternoon (NO LIE!!). As you can see, however, I am nearly done with the (very) notable exception of the product labeling piece. I also want to do a little more research into pricing and the managed care strategy to finalize those sections and I have a few more numbers to insert into the forecast chart -- but aside from that its just about there!!

I would like to set up a meeting to review this with you at the least, or you and Laura and whoever you think would be appropriate -- I think some of this content should be discussed and agreed upon rather than put forward by me unilaterally. (Unless I really am being foolish in thinking anyone will ever read this.....). Let me know what you think.

Thanks!
Andrea

594 development plan - commercial sections

J. Landsberg DEP. EX. NO. 4
FOR ID., AS OF 2-16-07 BC

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B. Marketplace: Chronic Neuropathic and Nociceptive Pain

B.1 a Neuropathic Pain Marketplace SWOT Analysis

Table B.1a includes a summary of the strengths, weaknesses, opportunities and threats associated with the information presented in this section with respect to the development of ABT-594.:

Table B.1a SWOT Analysis (Strengths/Weaknesses/Opportunities/Threats)		
CATEGORY	ITEM (Impact)	STRATEGY
Strengths	<p>Increasing incidence of diabetes and subsequent diabetic neuropathy market (Mod)</p> <p>Indication in diabetic neuropathy will likely lead to some spillover use in other neuropathic pain and chronic nociceptive pain (High)</p> <p>Bulk of competition is generic (Mod)</p> <p>Few products have indication for neuropathic pain limiting sales and marketing efforts (High)</p>	<p>Conduct or fund trials in neuropathic and chronic nociceptive pain beyond diabetic neuropathy</p> <p>Obtain indication for neuropathic pain (as broadly as possible)</p> <p>Capitalize on indication labeling through appropriate sales and marketing campaign</p>
Weaknesses	<p>Current leading treatment (gabapentin) perceived as effective, safe and well tolerated (High)</p> <p>Advances in the treatment of glycemic control could decrease the rate at which diabetic neuropathy occurs (Low in near term)</p> <p>Diabetic and other neuropathies are often underdiagnosed and mis/under-treated (Mod)</p> <p>Painful aspect of neuropathy is not always present or persistent (Mod)</p> <p>Limited regulatory history for indication (Mod)</p>	<p>Conduct trials to compare efficacy and tolerability to market leaders</p> <p>Monitor competitive landscape and adjust clinical development and marketing strategies appropriately</p> <p>Support screening and aggressive treatment of diabetic and other neuropathies</p> <p>Work closely with regulatory and plan for 'End of Phase II' FDA meeting</p>
Opportunities	<p>Large unmet need for effective treatments (High)</p> <p>Novel mechanism may generate increased excitement (Low)</p> <p>Increasing focus on aggressive treatment of pain (Mod)</p>	<p>Demonstrate equal or better efficacy to currently available agents</p> <p>Demonstrate equal or better tolerability to currently available agents</p>
Threats	<p>Gabapentin follow-on compound, pregabalin, may be even more effective and may pursue indication for neuropathic pain (High)</p> <p>Pricing pressure from managed care, government due to shift from low cost generics (Mod)</p> <p>Nicotinic association could decrease public acceptance and raise fears regarding addictive potential (Mod)</p> <p>Primary treatment aimed at neuropathic process could limit market for neuropathic pain agent (Low)</p>	<p>Maximize efficacy, safety and convenience of compound and formulation</p> <p>Conduct pharmacoeconomic studies and garner support of patient advocacy groups</p> <p>Develop and execute public relations plan to allay fears regarding nicotine</p> <p>Conduct studies to demonstrate non-addictive nature of compound</p>

B.1 b Chronic Nociceptive Pain Marketplace SWOT Analysis

Table B.1b includes a summary of the strengths, weaknesses, opportunities and threats associated with the information presented in this section with respect to the development of ABT- 594.:

Table B.1b SWOT Analysis (Strengths/Weaknesses/Opportunities/Threats)		
CATEGORY	ITEM (Impact)	STRATEGY
Strengths	Large, growing market consisting of primarily OA, RA and back pain (High) Large undiagnosed OA population to provide significant market growth (Mod) Increasing incidence of chronic pain conditions with aging population (Mod) Over 50% of chronic pain patients take a medication every day (Low)	Conduct trials in OA or other chronic nociceptive pain area for indication or publication Support screening and increased treatment of OA
Weaknesses	Competitors may not require titration to avoid AEs and therefore can be used PRN rather than limited to only those patients on persistent, daily therapy (Mod)	Work on formulation to minimize or eliminate need for titration
Opportunities	Significant unmet need for alternative to opioids that have equal efficacy with less side effects and no scheduling (High) "Ceiling effect" of NSAIDs and COX 2 competitors (Mod)	Conduct opioid sparing or opioid replacement trials Conduct studies to demonstrate non-addictive nature of compound Position 594 as 'bridging' compound after ceiling effect reached and before use of scheduled narcotics
Threats	COX -2s may be firmly entrenched as market leaders for all chronic pain conditions (Mod) Combination products combining opioids with non-opioid analgesics or potentiators may meet market demand for improved side effect profile and offer steep competition (Mod)	Demonstrate key benefits over current and potential competitors in terms of efficacy or safety Carefully position along pain severity spectrum to preserve a target patient population

B.2 Epidemiology/Disease Class

Pain is the most common symptom of disease and the most frequent complaint with which patients present to physicians. The economic burden of pain in the United States is estimated at \$100 billion a year in direct and indirect costs. Approximately 95 million Americans per year receive drug therapy for pain, which represents about 50% of those who suffer from pain. (more

appropriate below in market overview) Chronic pain, including both neuropathic and nociceptive pain, is considered to be the single most common cause of suffering and disability in the industrialized world with an estimated 25-30% of the population experiencing some form of chronic pain. Chronic neuropathic pain is a frequent sequelae (sp?) of diabetes, AIDS, and other viral infections, as well as 'entrapment' disorders such as carpal tunnel syndrome. Diabetes is increasing at an alarming rate in the United States, with an estimated 15 million type II diabetics in 2000, and, despite advances in treatment, the development of complications such as neuropathy remains significant. The diagnosed prevalence of diabetic neuropathy is estimated to be about 2 to 3 million patients, with at least 10 to 20% of those patients experiencing painful symptoms.

Chronic nociceptive pain categories include osteoarthritis, chronic back and neck pain, rheumatoid arthritis, and cancer pain and these diagnoses are expected to become more prevalent as the population ages. Current overall prevalence for these disorders is staggering, over 200 million worldwide, and, although the diagnosed and treated populations are lower, improved treatment options and awareness have the potential to drive significant growth. Osteoarthritis (OA) is one of the largest segments of the analgesia market, and one of the most common nociceptive pain conditions treated by primary care physicians and Over 35 million people worldwide suffer from OA, and three-fourths of OA sufferers surveyed indicate that the disease interferes with their daily activities. Estimates of worldwide sales of prescription analgesics to treat OA range from \$2.25-3 billion. According to a recent study, as many as 47% of Americans diagnosed with OA take a prescription analgesic at least occasionally for the condition. NSAIDs/COX-2s and acetaminophen are the standard treatments for OA. However, the new COX-2 inhibitors are expected to grow the OA market due to their expected higher levels of GI safety. This added safety would attract patients who were administered prescription or OTC NSAIDs only occasionally to avoid potentially severe gastric ulcerations and bleeding. The COX-2 inhibitors will also take share from branded and multisource prescription NSAIDs. As a result, the COX-2 inhibitors are expected to grow the OA market in prescriptions and sales, maybe by a significant amount.

A summary of the prevalence of relevant chronic pain diagnoses is shown in Table B.2c.

Diagnosis	Table B.2c Prevalence of Key Target Pain Diagnoses	
	Est. 2000 Prevalence (MM)	
	U.S.	Worldwide ³
Neuropathic Pain in Diabetic Neuropathy ¹	0.6	0.9
Postherpetic and Trigeminal Neuralgia ¹	0.5	0.7
Osteoarthritis ²	9.4	24.3
Chronic Low Back Pain ²	8.5	21.6
Rheumatoid Arthritis ²	1.9	2.9
Cancer Pain ²	1.0	1.2
Total for Key Pain Diagnoses	21.9	51.6

1. Decision Resources, 1999. Data reflect number of pain diagnoses such that a patient might be diagnosed with two pain diagnoses of different pain types at separate visits.
 2. Decision Resources, 1999 (Data presented reflects *diagnosed* prevalence)
 3. Germany, France, Italy, Spain, UK, and Japan.

B.3 Market Overview [Andrea/Laura to review]

Pain is the most common symptom for which individuals seek medical assistance. Pain is the primary complaint of 50% of all patients who visit a physician.

The economic burden of pain in the United States is estimated to be \$100 billion a year in direct and indirect costs. In 1996, the worldwide diagnosed pain population was 427 million, of whom 37% were from the U.S. and 63% from outside the U.S. Approximately 95 million Americans per year receive drug therapy for pain, which represents only about 50% of those who suffer from pain. Physician or patient concern about drug safety and side effect profiles, fear of addiction, the use of OTC therapies, or non-pharmacological treatments account for the 30-50% of patients who seek treatment for pain but are not prescribed an analgesic. Efforts to change this mindset, however, are likely to result in a greater percentage of sufferers receiving pharmacologic therapy. Pain specialists, advocacy groups and patients have campaigned vociferously for the more aggressive treatment of pain over the last decade. One trend toward acceptance of this standard is the 12% increase over prior year in 1999 sales of injectable narcotic agents. While much of the

effort has targeted physician and patient fears of opioid use, the primary goal is to treat pain more proactively and completely. (the above was the only example I could find) The great success of the recently launched COX-2 analgesics, achieved by growing the market with minimal erosion of the NSAID class, speaks to the increasing consciousness regarding pain management and the high unmet need for drugs that are safer, yet maintain equivalent efficacy, than those currently available. It is expected that, as improved treatments become available and awareness of the long term benefits of adequate pain management becomes widespread, the pain market will grow considerably. Total U.S. sales of prescription pain medications reached over \$5.1 billion in 1998.

Chronic pain sufferers may account for as much as 20% of the adult population implying over 130 million adults in the seven major pharmaceutical markets suffer from chronic pain. It is estimated that only one-fourth to one-half of chronic pain patients obtain inadequate pain relief. The chronic pain market can be segmented into two major groupings, neuropathic and nociceptive. Over the near term, the pain market is likely to grow. [Andrea to provide evidence of market growth in recent past and expectations for future]. The pain market can be segmented along several lines. A major division is between neuropathic and nociceptive pain. Chronic neuropathic pain includes the pain associated with diabetic polyneuropathy, post-herpetic neuralgia, sciatica, entrapment neuropathies (such as carpal tunnel syndrome), phantom-limb syndrome, and others. Chronic nociceptive pain includes pain associated with surgery, trauma, osteoarthritis, rheumatoid arthritis, lumbar spine disease, cancer, and other causes. Neuropathic and nociceptive pain differ in symptoms, pathophysiology and treatments.

Neuropathic pain is a large, yet largely untapped market. Estimates vary widely for the number of worldwide sufferers, from as low as 20 million to as high as 50 million or more. Estimates of the number of cases is limited by inadequate epidemiological studies. One report puts the total US prevalence of neuropathic pain at 4 million. Neuropathic pain is often treated with tricyclic antidepressants (TCAs), anticonvulsants (e.g. gabapentin) and alpha adrenergic agonists; collectively, these drug classes are sometimes referred to as "adjuvant pain medications". PCPs often still prescribe OTC analgesics or prescription NSAIDs for neuropathic pain even though there is little evidence for their usefulness in for this condition. US sales in 1999 for the key neuropathic pain treatments, Neurontin, carbamazepine, and tricyclic antidepressants (TCAs), are estimated to be \$350 million. This dollar market value likely underestimates this market's potential due to a number of factors. Only the anticonvulsant Tegretol (carbamazepine), which is off-patent, has a specific indication for neuropathic pain in the US (although Neurontin (gabapentin) recently received an indication in the UK for the treatment of neuropathic pain). Therefore there has been no funding from the pharmaceutical industry to improve diagnosis and

treatment of neuropathic pain and drive market growth. Of even greater impact on total market sales, most of the agents used to treat this population, with this exception of Neurontin, are low cost, generic products. ???Prescription drug sales for the treatment of neuropathic pain exceeded \$1 billion worldwide.???(Bruce: where did this come from? I cannot find anything to justify this number from the data and reports I have but am happy to go with it if we have a recent reference). In the U.S. alone, approximately \$250 million of the sales of the anticonvulsant Neurontin (gabapentin) are attributed to off label use for the treatment of neuropathic pain. A

Significant unmet need remains, however, in the treatment of neuropathic pain since few medications provide complete pain relief and most adjuvant medications have significant side effects. As the prevalence of the underlying disorders (diabetes, herpes zoster, etc) increases with the aging population and more effective and tolerable medications become available, the neuropathic pain market is expected to experience significant growth. The following tables show the factored U.S. and ex-U.S. prescription and sales volume for key neuropathic pain therapies 1999.

Table B.3a. 1999 Key Neuropathic Pain Products, Estimated TRxs				
Class	1999 U.S. TRx (MM)	U.S. TRx CAGR '97-'99	1999 ex-U.S. TRx (MM)	ex-U.S. TRx CAGR '97-'99
Neurontin	3.3	26.3%	N/A	N/A
Carbamazepine	1.0	12.6%	N/A	N/A
TCAs	8.2	1.1%	N/A	N/A
TOTAL	12.5	5.6%	N/A	N/A

Source: IMS, factored for neuropathic uses.
N/A = not available

Table B.3b. 1999 Key Neuropathic Pain Products, Estimated \$ Sales				
Class	1999 U.S. Sales (\$MM)	U.S. Sales CAGR '97-'99	1999 ex-U.S. Sales (\$MM)	ex-U.S. Sales CAGR '97-'99
Neurontin	\$308	28.7%	N/A	N/A
Carbamazepine	\$17	13.1%	N/A	N/A
TCAs	\$26	-3.3%	N/A	N/A
TOTAL	\$351	21.7%	N/A	N/A

Source: IMS, factored for neuropathic uses; Ex-U.S. data includes retail pharmacy data from all audited markets and hospital data from major European markets and Canada only.

Nociceptive pain is categorized by duration (acute or chronic) and by severity (mild, moderate, and severe). The mild and, to a lesser extent, moderate segments have multiple product entries and are generally well satisfied by OTC products such as aspirin, acetaminophen, ibuprofen and other NSAIDs/COX-2s. Prescription NSAIDs are generally written for chronic pain of moderate severity, though potentially serious GI or renal side effects may complicate treatment (COX-2s may be associated with fewer adverse events). The moderate and severe segments of the market have many opioid product offerings that are mostly generic, undifferentiated and inexpensive. Some branded opioids, however, have been very successful (OxyContin is projected to have 2000 revenues of \$1 billion). Many patients, however, develop tolerance to these drugs. In addition, opioids are scheduled, a regulatory status that creates administrative burdens and barriers to prescribing. These barriers are particularly high in European markets. As a result, opioid use in Europe is restricted almost entirely to cancer pain and there exists a large unmet need for effective treatment of severe pain. While opioids and combination opioids accounted for the majority of analgesic prescriptions at 55%, NSAIDs had the highest share of total prescription analgesic sales at 37%.

~~{the following section has been updated to reflect the new organization of this section into neuropathic and nociceptive pain, but the market segmentation parallels to the IMS data must be verified and updated...i.e., originally, this section was a discussion of the three classes of analgesics without reference to nociceptive per-se}~~

The prescription market for nociceptive pain is made up of at least three four key classes of analgesics: NSAIDs, COX-2s, Opioids (and combination products), and Other Non-Opioids (including aspirin, acetaminophen, and synthetic non-opioids). Anesthetics, anti-migraine and adjuvant medications are not included in this market definition. The following tables show U.S. and ex-U.S. prescription and sales volume for key pain classes for 1999.

Table B.3c. 1999 Key Prescription Nociceptive Pain Products, TRxs

Class	1999 U.S. TRx (MM)	U.S. TRx CAGR '97-'99	1999 Ex-U.S. TRx (MM)	Ex-U.S. TRx CAGR '97-'99
NSAIDs	70.7	-1.4%	N/A	N/A

COX-2s	22.4	N/A	N/A	N/A
Opioids ¹	154.2	2.5%		
Other Non-Opioids ²	45.5	-0.9%	N/A	N/A
TOTAL	292.8	0.8%	N/A	N/A

Source: IMS
N/A = not available or not applicable
¹Includes IMS groups: Morphine, codeine and combos, propoxyphene, synthetic narcotics (injectable and non-injectable)
²Includes IMS groups: Synthetic non-narcotics, aspirin, acetaminophen (injectable and non-injectable)

Table B.3d. 1999 Key Prescription Nociceptive Pain Products, \$ Sales

Class	1999 U.S. Sales (\$MM)	U.S. Sales CAGR '97-'99	1999 ex-U.S. Sales (\$MM)	ex-U.S. Sales CAGR '97-'99
NSAIDs	\$1,565	-3.2%		
COX-2s	\$1,558	N/A		
Opioids ¹	\$1,887	7.7%		
Other Non-Opioids ²	\$1,337	-4.5%		
TOTAL	\$6,347	4.3%		

Source: IMS (excludes injectables)
¹Includes IMS groups: Morphine, codeine and combos, propoxyphene, synthetic narcotics (injectable and non-injectable)
²Includes IMS groups: Synthetic non-narcotics, aspirin, acetaminophen (injectable and non-injectable)
Ex-U.S. data includes retail pharmacy data from all audited markets and hospital data from major European markets and Canada only.

NSAIDs and COX-2s are generally used in chronic nociceptive pain syndromes and when pain severity is of mild to moderate intensity. NSAIDs/COX-2s exhibit analgesic and mild anti-inflammatory properties, and are drugs-of-choice in such pain conditions as osteoarthritis, rheumatoid arthritis and lower back pain. NSAIDs/COX-2s have fewer central nervous system side effects than opioids. NSAIDs, however, can cause potentially serious renal and gastrointestinal side effects, including gastric ulceration and bleeding. COX-2s may appear to have a lower rate of these adverse events, due to increased selectivity of action. However, current COX-2s do not eliminate the risk of GI complications completely. but experience with COX-2 is limited to the past year. Another drawback of NSAIDs/COX-2s is the presence of a

'ceiling effect' in which even additional amounts of drug fail to increase analgesic activity. This factor often leads to the use of stronger analgesics such as opioids.

(reordered) In the U.S., opioid analgesics are considered the drugs-of-choice for acute nociceptive pain, especially of moderately-severe to severe intensity. Physicians often avoid prescribing opioids for chronic pain conditions due to fear of tolerance and addiction, although opioids are the most commonly prescribed medication for moderate to severe cancer pain. Ex-U.S. opioid use varies considerably by country. Physicians in Scandinavia, the UK, France and [Japan-verify] are more likely to prescribe opioids compared to other ex-U.S. countries and prescriptions have increased considerably over the past 5 years. In Italy, Spain and Germany, opioid use is extremely restricted, requiring patient identity cards and special prescription forms that must be obtained, in person, by the physician; morphine is often considered a last resort. In both the U.S. and ex-U.S., opioids are government-scheduled products with restricted prescribing and product distribution.

"Other non-opioids" Non-narcotics include are defined as (1) non-opioid/non-NSAID agents like aspirin, acetaminophen or tramadol, and (2) NSAIDs that are positioned and marketed as analgesics, such as ketorolac or bromfenac sodium. These non-narcotics are generally used in place of opioids to treat moderate pain, or in some cases, moderately-severe pain.

Most analgesics are indicated for the treatment of one or more specific nociceptive pain states (e.g. osteoarthritis). Depending on its characteristics, however, a significant number of a product's prescriptions may come from non-indicated pain states (i.e., spillover prescriptions). A product indicated for osteoarthritis, for example, is likely to be prescribed for chronic lower back pain, rheumatoid arthritis, and other pain states with similar clinical characteristics or etiologies. Efficacy in osteoarthritis has become a benchmark for analgesic efficacy in most chronic nociceptive pain states of mild to moderately severe intensity.

B.4 Current Treatment Options

TABLE B.4A CURRENT TREATMENT OPTIONS: NEUROPATHIC PAIN

Category	Drug Class	Mechanism of Action	Pain Treated	Issues
Antiepileptics as analgesics*	Gabapentinoids (gabapentin)	Unknown	Distal symmetric neuropathic pain (diabetes, HIV, idiopathic, etc.) Post herpetic neuralgia (PHN)	<u>Strength:</u> Effective, well tolerated, not metabolized, no drug interactions <u>Side effects:</u> Dizziness at high doses <u>Other drawbacks:</u> No neuropathic claim in US; cost; modest analgesic effect, titration
	Iminostilbenes (carbamazepine)	Slows voltage-gated Na^+ channel activation recovery	Trigeminal neuralgia	<u>Strengths:</u> Very effective, inexpensive <u>Side effects:</u> Ataxia, dysmetria, unsteadiness, hepatotoxicity, aplastic anemia, hypersensitivity reactions <u>Other drawbacks:</u> Drug interactions
Antidepressants as analgesics	Tricyclic antidepressants (amitriptyline, nortriptyline)	Probably inhibit biogenic amine reuptake	Distal symmetric neuropathic pain (diabetes, HIV, idiopathic, etc.) Post herpetic neuralgia (PHN)	<u>Strengths:</u> Modest analgesic effect, inexpensive <u>Side effects:</u> Anti-cholinergic (dry mouth, sedation), cardiac arrhythmia, weight gain <u>Other drawbacks:</u> Cardiac effects, titration
	Mixed serotonin and norepinephrine reuptake inhibitors (venlafaxine)	Mixed serotonin and norepinephrine reuptake inhibitors (venlafaxine)	Distal symmetric neuropathic pain (diabetes, HIV, idiopathic, etc.) Post herpetic neuralgia (PHN)	<u>Strengths:</u> Modest analgesic effect, inexpensive? <u>Side effects:</u> Anti-cholinergic (dry mouth, sedation), cardiac arrhythmia <u>Other drawbacks:</u> Cardiac effects, titration
Miscellaneous	Opioid and norepinephrine reuptake inhibitor (tramadol)	Opioid and norepinephrine reuptake inhibitor	Distal symmetric neuropathic pain (diabetes, HIV, idiopathic, etc.) Post herpetic neuralgia (PHN)	<u>Strengths:</u> Moderate pain relief without the opiate stigma, non-scheduled <u>Side effects:</u> Nausea, vomiting, sedation <u>Other drawbacks:</u> May reinitiate physical dependence in previously opioid-dependent patients. May eventually receive scheduled status

* Many newer antiepileptic agents (e.g., Tiagabine, lamotrigine) have recently or will soon undergo clinical trials in neuropathic pain.

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TABLE B.4B CURRENT TREATMENT OPTIONS: NOCICEPTIVE PAIN

Category	Drug Class	Mechanism of Action	Pain Treated	Issues
Opioid	Opioids (e.g., morphine, codeine)	Opioid receptor activation	Surgery, injuries, musculoskeletal disorders, cancer Moderate to severe pain Opioids are the drugs of choice for severe acute pain and cancer pain	Strength: Potent analgesic effect, inexpensive Side effects: Constipation, Nausea and Vomiting, Sedation, Cognitive Impairment, Respiratory Depression, Pruritis Other drawbacks: Development of tolerance, addiction potential, scheduled drugs, do not reduce inflammation
	Opioid Combination with another analgesic (e.g., aspirin or acetaminophen)	Opioid receptor activation Combination preparation offsets opioid side effects by adding second analgesic with a different mechanism of action	Surgery, injuries, musculoskeletal disorders Moderate to severe pain	Strength: Potent analgesic effect, and depending on combination agent, may also decrease inflammation and body temperature; reduced opioid side effects Side effects: All effects associated with each of the drugs administered, although reduced in frequency and severity Other drawbacks: All drawbacks associated with each of the drugs administered
Non-Opioid	NSAIDS	Inhibit the synthesis of prostaglandins, which are responsible for inflammation, increased body temperature, and sensitization of pain receptors	Osteoarthritis, rheumatoid arthritis, lower back pain, and other chronic pain conditions in addition to some mild to moderate acute pain conditions	Strength: Fewer CNS side effects than opioids, and no addiction potential, inexpensive Side effects: Gastric ulceration and bleeding Other drawbacks: Ceiling effect (complete pain relief cannot be achieved even after dose escalation)

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TABLE B.4B CURRENT TREATMENT OPTIONS: NOCICEPTIVE PAIN

Category	Drug Class	Mechanism of Action	Pain Treated	Issues
Non-Opioid (con't.)	COX-2 Inhibitors (celecoxib)	Inhibit the synthesis of prostaglandins, which are responsible for inflammation, increased body temperature, and sensitization of pain receptors Preferential COX-2 vs. COX-1 inhibition may reduce risk of GI interaction		<u>Strengths:</u> Claim fewer GI side effects than NSAIDS with similar analgesic effect <u>Side effects:</u> Peripheral edema <u>Other drawbacks:</u> cost
	Acetaminophen	Mechanism of action is poorly understood, but appears to involve effects in the CNS (has analgesic and antipyretic effects)	Sprains, strains, injuries, musculoskeletal pain, osteoarthritis Management of mild to moderate pain	<u>Strengths:</u> Has no effects on platelet function, has no GI toxicity, has fewer CNS side effects than do opioids, inexpensive <u>Side effects:</u> May be hepatotoxic in heavy drinkers and patients with liver disease <u>Other drawbacks:</u> Lacks anti-inflammatory activity. Ceiling effect (complete pain relief cannot be achieved even after dose escalation)
Miscellaneous	Opioid and norepinephrine reuptake inhibitor (tramadol)	Dual mechanism of action via opioid and non-opioid mechanisms (norepinephrine reuptake inhibitor)	Used in the treatment of moderate to severe pain	<u>Strengths:</u> Moderate pain relief without the opiate stigma, non-scheduled <u>Side effects:</u> Nausea, vomiting, sedation <u>Other drawbacks:</u> May reinitiate physical dependence in previously opioid-dependent patients. May eventually receive scheduled status

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B.5 Competitive Analysis – Emerging Competition [Andrea/Laura to review]

Almost 100 compounds are currently in development for prescription pain management, though some of these compounds are also being developed for other non-analgesic indications. The majority of the analgesic compounds in the pipeline represent incremental improvements to the opioids or NSAIDs, or consist of new formulations or delivery mechanisms for the standard analgesics. Fewer than 30% of the compounds in development have novel mechanisms of action. Drugs with novel mechanisms are expected to provide the bulk of the promoted competition for ABT-594.

Among the novel agents in development, the greatest threat to ABT-594 is likely to be posed by other nicotinic compounds in development for pain. ABT-594, now in Phase IIb trials, is suspected to be the most advanced nicotinic compound in the analgesia pipeline. The first nicotinic compounds from competitors to be launched in the class may be for Alzheimer's Disease or Parkinson's Disease. These compounds do not represent a threat to ABT-594, unless significant safety concerns or evidence of tolerance, dependence or abuse are an issue and become associated with the class as a whole.

The pipeline for the treatment of neuropathic pain does not have a blockbuster compound on the order of the COX-2 inhibitors. However, pregabalin, the follow-up to Parke-Davis' Neurontin (gabapentin), is expected to perform well; analyst reports predict its sales for neuropathic pain may be almost \$100 million by 2003, its second year post expected launch. Initial data from pregabalin suggests a compound that overcomes the absorption and uptake limitations associated with gabapentin leading to a more convenient dosing schedule and resolved 'ceiling effect'. However, increased doses and corresponding increased plasma levels appear to be associated with greater efficacy and more frequent adverse events. The marketing and sales power of Pfizer is likely to drive the product to success, despite such concerns.

For the treatment of osteoarthritis (OA), the COX-2 inhibitors represent the most significant competition, with sales of as much as a staggering \$13 billion by 2004 being predicted. Use beyond pain into colorectal cancer and neurodegenerative disorders is also being explored for COX-2s. Searle and Merck both have follow-up compounds well along in development which purport to have greater selectivity for COX-2 vs. COX-1 and therefore offer the potential for increased potency and decreased side effects. Other second generation COX-2s are in the pipeline, although J&J recently announced the decision to stop development of Japan Tobacco's compound JTE 522. Unresolved side effect issues surrounding COX-2 inhibitors remain,

however, including the risks of thrombosis, hypertension, reproductive dysfunction and teratogenicity that may show up as the exposure to these agents becomes more widespread. The launch of Searle's Celebrex (celecoxib) in January 1999 is one of the most successful product launches in industry history. After ten weeks on the market, prescriptions for Celebrex represented 24% of new NSAID prescriptions. Merck's Vioxx (rofecoxib), approved in May 1999 is also expected to be a very successful product in the treatment of OA as well as other pain states.

Table B.5a. Analgesia Pipeline – Key Novel Agents				
Product	Company	Mechanism	Phase	Comment
pregabalin	Parke-Davis	Ca channel blocker	III	Neuropathic pain, chronic pain Follow-up to Neurontin
saredutant	Sanofi	NK-2 receptor antagonist	II	General pain MOA losing favor; active program?
ZD4952	Zeneca	prostaglandin receptor antagonist	II	Moderate to severe pain
GV196771	Glaxo	glycine antagonist	II	Chronic pain, showing promise
tepxoxalin	J&J	COX/5-LO inhibitor	II	OA, described as 'steroid replacing anti-inflammatory drug'
darbufelone	Parke-Davis	COX/5-LO inhibitor	II	General pain
HCT-3012	NicOx	Nitric oxide NSAID	I	Pain and inflammation
cizolirtine	Esteva	Substance P	II	Anaesthesia, antipyretic
Others??				
Sources: ADIS, IMS, Decision Resources, company reports				

Table B.5b. Development Pipeline – Nicotinic Mechanisms			
Product	Company	Phase	Comment
GTS-21	Taiho	II	Target is Alzheimer's Disease May have preclinical pain program; looking for partner
CMI 980	Cytomed	Preclinical	Target is pain Epibatidine analog

SIB-T1887	Sibia	Preclinical	Target is pain
FID 072021	Fidia	Preclinical	Target is pain; not actively funding

Sources: ADIS, IMS, company reports

B.6 Unmet Needs [Andrea/Laura to review]

In general, a significant unmet need exists for safer, non-abusable, non-addicting, non-tolerance producing, and non-scheduled efficacious oral and parenteral analgesic products for the treatment of moderate to severe neuropathic and chronic nociceptive pain.

Table B.6. Unmet Market Needs and the Impact of the Pipeline	
Unmet Need	Pipeline Impact
Efficacy in moderate to severe pain without tolerance, dependence or abuse	Novel nicotinic agents like ABT-594 may provide efficacy in more severe pain states without opioid-like liabilities
Efficacy in neuropathic pain	Pregabalin may provide incremental improvement in neuropathic pain efficacy over gabapentin, but may also have increased frequency of adverse events Novel nicotinic agents like ABT-594 appear to have efficacy in neuropathic pain, based on animal models
Reduction in the GI bleeding risk of NSAIDs	COX-2 inhibitors appear to reduce the incidence and severity of GI ulcers and bleeding; second generation COX-2s may increase therapeutic window further but Celebrex retains labeled warnings regarding ulceration comparable to traditional NSAIDs
Overcome ceiling effect of NSAIDs	Preclinical studies did not indicate a ceiling effect for novel nicotinic agents like ABT-594
Extended dosage intervals or novel delivery mechanisms for improved compliance and convenience	Once weekly dosing formulations being explored for COX-2s, etc. Patch technology improvements likely
Therapies aimed at disease modification, prevention	Agents that decrease rate of diabetic complications (eg aldose reductase inhibitors) or directly treat neuropathy (bimoclomol) may decrease incidence of neuropathic pain

C. Product Positioning

C.1 Product Positioning Options [Andrea/Laura to review]

Table C.1a includes a summary of the strengths, weaknesses, opportunities and threats associated with the information presented in this section with respect to the development of ABT-594.

Positioning alternatives/options	Strategy	Strengths	Weaknesses
Equal efficacy to Neurontin and TCAs in neuropathic pain with improved dosing, AEs, and safety	Sell against top neuropathic pain products on convenience, tolerability and safety	Efficacy to date supports BID, possibly QD dosing Low level of CNS AEs No weight gain	May have too high level of nausea and vomiting to compete with Neurontin (pregabalin?) on AEs
Better efficacy than Neurontin and TCAs with comparable dosing, AEs and safety	If AEs for ABT-594 too frequent vs. competition, sell on 'power'	Efficacy data likely to support May be better fit with AE profile	Neurontin and TCAs <i>perceived</i> to have high efficacy; may not be able to match Neurontin's perception as extremely safe and well tolerated
The only oral agent indicated for the treatment of neuropathic pain	Capitalize on 'government approved' status to increase prescriber confidence	Data to date supports efficacy in neuropathic pain Current timeline gives ABT-594 neuropathic pain indication by mid 2004	Pregabalin (or others?) may be to market first with neuropathic pain indication Neuropathic pain indication still uncertain from regulatory standpoint
Equal efficacy and safety to COX-2s without ceiling effect	Attempt to enter into large COX-2 market	No ceiling effect seen with ABT-594	May limit use to <i>after</i> COX-2 failure COX-2 agents will be firmly entrenched
Opioid-like efficacy without addictive potential and with fewer AEs than opioids for treatment of moderate to severe chronic pain	Capitalize on market reluctance to use opioids by providing safe, efficacious alternative	Provides clear, compelling reason to use and matches product profile to date	May niche ABT-594 to more severe patients and limit market

“General” pain	Requires data to support acute (molar extraction and post-surgical pain) and chronic claims	Would create a drug for most kinds of pain	ABT-594’s analgesic onset is too delayed for acute use
Chronic pain	Requires data from chronic pain states, but pain states not currently associated with indications (not osteoarthritis, not cancer; acceptable data might include low back pain, fibromyalgia); does not include neuropathic pain	Label would support use in the wide variety of chronic pain (large population)	Regulatory paradigm untested and pain states specified represent high risk trials
Neuropathic pain	Submit data on diabetic neuropathy pain. Phase IV to extend to other neuropathic pain disorders (e.g., PHN)	Would address significant unmet needs; add smaller neuropathic segments later	Regulatory paradigm untested
Disease specific claim—osteoarthritis	Submit or publish data in osteoarthritis to demonstrate ABT-594’s efficacy in a chronic nociceptive pain state. Because osteoarthritis is a well recognized model of pain, market research predicts significant use in other chronic nociceptive pain states based upon osteoarthritis data alone	Label would specifically support use in osteoarthritis, a large but fairly well reviewed market. Off label use may extend to entire chronic nociceptive market. Publication alone in osteoarthritis may provide basis for off-label use in entire nociceptive market (with subsequent publication in other chronic nociceptive pain states)	Fairly well served market

C.2 Target Product Profile [Andrea/Laura to review]

C.2.1 ABT-594 Target Product Profile

Table C.2.1 below, outlines the desired target product profile for ABT-594:

Table C.2.1. ABT-594 Target Profile					
PPCC/DDC Profile (12/10/97)	Current Profile (8/00)	Rationale for Profile Change	Probability	Status	Share Impact
Indicated for the treatment of pain (general pain claim)	Indicated for the treatment of osteoarthritis pain	"General pain" claim not achievable due to slow onset of action; proof of principle established in molar extraction study Indication specific claims now favored since general pain claim not achievable	Medium	9/99, 1Q01	High
Effective in neuropathic pain	Indicated for the treatment of neuropathic pain	Indication specific claims now favored since general pain claim not achievable	?Low	9/99, 2Q01	Medium
Effective for moderate to moderately-severe pain	N/A	No longer applicable without general pain, acute or chronic pain (not otherwise specified) claims??	N/A	N/A	N/A
Not scheduled/no abuse potential?	No change	N/A	High	4Q02	High
Improved safety profile compared to opioids including: - less GI motility impairment - less respiratory depression - low tolerance potential - no dependence/withdrawal	No clinically significant tolerance, dependence or withdrawal In contrast to opioids, no constipation or respiratory depression liability Tolerability comparable to currently used neuropathic and chronic nociceptive pain products	Simplify profile to focus on the most commercially important AEs Need to be well-tolerated to sell in crowded market with many alternatives	Medium	2Q01	High
	Very few abnormal LFTs	Abnormal LFTs in a few Phase I subjects	High	9/99	High
	Very low nausea/vomiting at effective dose	Incidence of nausea/vomiting in single dose Phase I & II subjects (food and dose dependent) similar to opioids	Medium ?Low	9/99	High
	Other safety OK	Simplify profile	Medium	9/99,	High

				2Q01	
	No significant or sustained differential efficacy in nicotine users vs. non-nicotine users	No difference seen in efficacy to date	Low?? HIGH?	9/99, 2Q01	High ?Med
	No significant or sustained differential negative side effect profile in nicotine users vs. non-nicotine users	Lower incidence of AEs in nicotine users in Phase II trial	High	9/99, 2Q01	Medium
	No re-initiation of cravings in ex-nicotine users	Possible due to nicotinic mechanism	Medium	2Q01	High
Onset of action in less than 30 minutes	Onset of action at 1.5 to 2 hours	Onset of action estimated at 90 minutes in Phase II trial	Low??	9/99	Medium
BID/TID dosing	BID/QD dosing	Competitive dynamics highlight importance of dosing convenience	High ?med	9/99	Medium
No major drug interactions, especially with drugs used for common chronic conditions	No change	N/A	High	4Q00	Medium

C.2.2 Target Product Label

Label Requirement	Desired Label claim/ Minimally Acceptable Criteria for a Commercially Viable Product/Competitive Advantage	Regulatory Requirements	Studies/Activities/Other strategy to Achieve
DESCRIPTION			
Formulation			
Dose form			
Dose strength(s)			
Route of Administration			
CLINICAL PHARMACOLOGY			
Pharmacodynamics			
Pharmacokinetics			
Absorption/Bioavailability			
Distribution			
Protein binding			
Distribution			
Metabolism			
Elimination			
Special Populations			
Effect of age			
Effect of gender			
Effect of race			
Use in pregnant women			
Use in Nursing Mothers			
Effect of concomitant disease			
Plasma Levels and clinical effect			
Effect of food on absorption			
Clinical Trial Data (by indication)			
Phase 3 studies			

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INDICATIONS AND USAGE			
Clinical Trial Data (only for one indication, the rest in C.P.)			
CONTRAINDICATIONS			
CONTRAINdications			
WARNINGS			
Black box warnings			
General Warnings (e.g., thrombocytopenia)			
Usage in Pregnancy			
PRECAUTIONS			
General			
Information for Patients			
Lab Tests			
Drug Interactions			
Drug/Lab Test Interactions			
Carcinogenesis			
Mutagenesis			
Impairment of Fertility			
Pregnancy			
Nursing Mothers			
Pediatric			
Geriatric			
ADVERSE REACTIONS			
Controlled Phase III study data (by indication)			
Other patient populations			
OVERDOSAGE			
OVERDOSAGE			
DOSAGE AND ADMINISTRATION			
By indication (dose/levels/length of treatment)			
Monitoring of Patients			
General dosing advice			
HOW SUPPLIED			
HOW SUPPLIED			

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C.2.3 Desired Promotional Claims

Table C.2.2 below, outlines the minimally acceptable criteria for a commercially viable product for ABT-594. Items in shaded boxes are NOT FUNDED.

C.2.2 Desired key messages should follow.

Desired key message	Regulatory requirement	Measure	Timing	Study Number	Type of message	Probability	Share Impact	Comments/Notes
Significantly Reduces pain associated with diabetic neuropathy	At least 2 adequate, well controlled studies	11 point Likert pain intensity	Launch	Phase III studies (TBD)	Efficacy	Low	High	
Efficacy and tolerability comparable to Neuronan and/or TCAs in neuropathic pain	At least 1 adequate, well controlled, comparative study	Acceptable pain scale, QOL, or numeric scale (EDDS if available)	Within 1 year of launch	Phase IV (TBD)	Efficacy, tolerability, patient satisfaction	Low	High	High risk but may be necessary to capture significant share especially if pain scale indicated. Difficult to conduct due to geographical restrictions indicated.
Significantly Reduces pain associated with osteoarthritis	At least 2 adequate, well controlled studies	WOMAC, 4-point categorical pain intensity	Launch or ASAP if launch with neuropathic pain indication	Phase III studies (TBD)	Efficacy	Medium	High	
Efficacy and tolerability comparable to COX-2s and/or ibuprofen in OA	At least 1 adequate, well controlled, comparative study	Acceptable pain scale, QOL, or numeric scale (EDDS if available)	Within 1 year of launch	Phase IV (TBD)	Efficacy, tolerability, patient satisfaction	Low	High	High risk but may be necessary to capture significant share.
No clinically significant tolerance, dependence or withdrawal	Phase I/II trials; specialized addiction studies	AE reports, specific addiction measures	Launch	All studies	Safety	Medium	High	
Well tolerated in comparison to -in contrast to opioids, with no constipation or respiratory depression liability	Phase I/II trials	AE reports	Launch	All studies	Safety	Medium	High	

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Desired key message	Regulatory requirement	Measure	Timing	Study Number	Type of outcome	Probability	Share Impact	Comments/Risks
Competitive rate of nausea and vomiting given level of efficacy Well tolerated in comparison to commonly used pain medications	Phase I/II trials	AE reports and efficacy measures	Launch	All studies	Safety	Medium	High	
Easy to use with BID/QD dosing and minimal titration	Phase I/II trials, market research	Study protocols, patient surveys, MD market research	Launch	All studies	Convenience and compliance	High	High	
Cost effective	Phase III and IV	Pharmacoeconomic data	Launch or shortly thereafter	TBD	Cost	Medium	Medium	Important for MC formulary acceptance
Higher patient satisfaction than other comparable medications	Phase III and IV	Survey, QoL measures (HEDIS if available)	Launch or shortly thereafter	TBD	Satisfaction	Medium	Medium	
No clinically relevant drug interactions	Preclinical? Phase III trials	Clinical and pre-clinical measures?	Launch	All studies	Safety and convenience	Medium	Medium	
Safe for long term use	Phase III extension	AE reports	Following launch?	TBD	Safety	Medium	Medium	

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C.3 Reimbursement/Pricing Strategies [Andrea/Laura to review]**C.3.1 Reimbursement/Managed Care**

Pricing trends in the U.S. and European markets will remain relatively stable in the short term due to two factors. First, the effect of higher-priced branded products entering the market in each analgesic class is tempered by the loss of patent protection of other branded products, and the resulting price erosion due to generic competition. Secondly, the large size of the prescription pain market tends to absorb the impact of individual products' prices in each analgesic class. The tremendous success of the COX-2 launches, with prices xxxxxxxx in comparison to their competition, demonstrate the xxxxxx price sensitivity of this market. do average price analysis

In the long term, however, the entry of several higher-priced novel analgesics may create an upward trend in prescription analgesic prices. Reaction from government and managed care payors to rising costs could create pressure to hold prices down. A large percentage of pain medications are government paid, reflecting the age and disability of pain patients; the future political impact on this market remains uncertain.

Due to the competitiveness of the pain management market, ABT-594 must favorably complete outcomes and pharmacoeconomic studies in order to gain significant formulary acceptance and use in managed care organizations (MCOs) and institutional settings. Positioning ABT-594 against analgesic procedures (eg: epidurals), would provide argument for MC acceptance but potentially niche the product to severe pain market. It is likely that substantial rebating will be necessary if the chronic nociceptive pain market is targeted; if neuropathic pain is primary focus, more price flexibility may be present due to the smaller patient population and high level of unmet need. Marketing research and consultation with the PPD managed care department will help determine the appropriate number of studies, comparators and desired endpoints. Inclusion of these measures into Phase III trials is key for the early acceptance and success of this product.

Table C.3.1. Reimbursement/Managed Care		
Pricing Strategies	Requirements/Status (i.e. met or unmet)	Strategy to Achieve
US • Third party/MCO reimbursement • Managed care • Formulary acceptance • 3 rd party payors • Government reimbursement Medicare/Medicaid	• Unmet • Unmet • Unmet	• Quality of life and pharmacoeconomics end points in Phase III studies • Pharmacoeconomic model • First in class
Europe •	• Unmet	
Japan •	• Unmet	

C.3.2 Pricing Strategy [Andrea/Laura to complete]

a. U.S.

The impact of COX 2s

b. Rest Of World

C.4 Sales Forecast(s) for ABT-594 [Andrea/Laura to update]

C.4.1 U.S. Sales Forecast

The U.S. sales forecast for the neuropathic and chronic persistent pain market is shown in Table C.4.1, below.

Table C.4.1 U.S. Forecast (Date of Forecast: 7/00)					
	2004	2005	2006	2007	2008
Chronic Persistent Nociceptive (OA) Market Rx's (MM) - % chg	18.4 3.5%	19.0 3.5%	19.7 3.5%	20.4 3.5%	21.1 3.5%
Neuropathic Market Rx's (MM) - % chg	10.7 5%	11.3 5%	11.8 5%	12.4 5%	13.0 5%
Abbott Share CPN(%)	1%	3%	6%	8%	10%
Abbott Share NP(%)	4%	8%	12%	16%	20%
Abbott Rx's CPN(000)	165	544	1,183	1,632	2,111
Abbott Rx's NP(000)	427	903	1,418	1,986	2,606
Price/Rx (WAC) (2%/year increase)	\$73.40	\$74.90	\$76.40	\$77.90	\$81.10
Abbott Sales (\$MM)	\$39.4	\$98.2	\$166.7	\$236.5	\$314.5
R&D (\$MM)	18	8	3	3	3
SG&A (\$MM)					
SMM (%)					
Div. Margin (\$MM)	(\$39.6)	\$31.2	\$106.8	\$174.7	\$252.1

10 year pre-tax NPV @ 12.5% = \$1,016 B

10 year post-tax NPV @ 12.5% = \$587 MM

Key forecast assumptions:

- First in-class ChCM-Neuronal Nicotinic Receptor compound for pain to market
- Indicated for treatment of neuropathic pain; publication on use, or indication, in OA in 2006
- Effective in neuropathic pain—No addictive potential
- Titration of 3-5 days
- Efficacy equal to gabapentin, ibuprofen
- Good tolerability and safety profile; comparable to gabapentin, COX-2s
- Peak share 20% in neuropathic pain, 10% in chronic, persistent nociceptive pain
- NDA Filed 5/03, Launch 5/04
- Cost comparable to Neurontin
- Usage = 70% chronic and 30% acute
- Weighted average days per Rx = 15.6
- Stocking at 8% of first year's sales
- Physician targets: D6-10 Neuros, D3-10 Rheumatologists/Endocrinologists, D9-10 PCPs
- Sampling at 80% of details at launch, 5 units per detail, 7 days of therapy per unit
- Significant promotional and PR spend in early years
- Significant payor discounting

- Patent expires 12/2016

Forecast Update Plan:

Forecast will be updated pending analysis of Phase IIb clinical trial results (March or April 2001) or before if the clinical trial plan changes from current assumptions. ~~in late June/early July 1999 to account for revised indications of OA and/or neuropathic pain and the associated spillover use in other pain states. Forecast will be available well in advance of ABT-594 Go/No-Go decision in 9/99.~~

C.4.2 Ex-U.S. Sales Forecast

The Ex-U.S. sales forecast is shown in Table C.4.2, below.

Table C.4.2 Ex-U.S. Forecast (Date of Forecast: 6/98)					
	2004	2005	2006	2007	2008
Market Rx's (MM) - % chg	-	-	-	-	-
Abbott Share (%)	1%	2.5%	3.8%	4.5%	5.0%
Abbott Rx's (MM)	-	-	-	-	-
Price/Rx (\$)	-	-	-	-	-
Abbott Sales (\$MM)	60	150	250	300	320
R&D (\$MM)	3.4	3.2	2.8	2.4	2.0
SG&A (\$MM)	27	53	50	48	45
SMM (%)	95%	95%	95%	95%	95%
Div. Margin (\$MM)	26	85	182	235	251

10 year pre-tax NPV @ 12.5% = \$428

10 year post-tax NPV @ 12.5% = \$253

Key assumptions:

- First in class ChCM
- Indicated for treatment of moderate to moderately-severe pain
- Effective in neuropathic pain
- Good tolerability and safety profile
- ~~No~~ no etinoinic effects (impossible as then wouldn't work!) No addictive potential
- Launched in all AI regions, including Japan, simultaneously (2003)

Forecast Update Plan:

Forecast will be updated 9/99 (in time for the Go/No-Go decision) to reflect results of marketing research to be conducted 3Q 1999 regarding expected uptake of 594 in OA and neuropathic pain markets, as well as potential spill-over prescribing for other pain states.

C.4.3 Global Sales Forecast

The global sales forecast is shown in Table C.4.3, below.

Table C.4.3 Global Forecast					
	2003	2004	2005	2006	2007
U.S. Sales (\$MM)					
Ex-U.S. Sales (\$MM)					
Total Sales (\$MM)					
Total Division Margin (\$MM)					

10 year pre-tax NPV @ 12.5% = \$B

10 year post-tax NPV @ 12.5% = \$ MM

C.5 Facilitating Launch and Market Penetration [Andrea/Laura to review]

Physicians, including neurologists, pain specialists, rheumatologists, and PCPs/internists/GPs, use analgesics in various pain states based upon efficacy in representative pain states such as diabetic neuropathy pain or osteoarthritis pain. Quantitative market research performed in 1999 demonstrated dramatic off label use in pain states similar to diabetic neuropathy pain and osteoarthritis where physicians are presented with an indication in these states alone.

C.5.1 Activities to Facilitate Launch	
ACTIVITY	PURPOSE
Phase III studies in diabetic neuropathy pain	Demonstrate efficacy in a reference pain state that creates a foundation for efficacy in all neuropathic pain states
Phase III studies in osteoarthritis	Demonstrate efficacy in a reference pain state that creates a foundation to efficacy in all chronic nociceptive pain
Pain Specialist Advisory meetings	Permits up to date knowledge of market science and pain treatment trends while building base of supportive, receptive opinion leaders with in-depth knowledge of ABT-594 (and entire neuronal nicotinic receptor program)
Medical education	Primes market with information regarding advances in pain management and introduces neuronal nicotinic receptor class to speed market familiarity and uptake
Information dissemination to publishers	Allows for discussion of class to be included in texts, professional newsletters, pharmacy alerts, etc. to build awareness and understanding of technology (NNR) pre-launch
Managed Care Director Advisories/Roundtables	Allows Abbott to gain understanding of reimbursement environment for pain products, key data that MCOs will need for formulary decisions to potentially include in Phase III clinical trial design
Publication of NNR and ABT 594 specific data at key meetings and in professional journals	Prime market with information regarding advances in pain management and introduce neuronal nicotinic receptor class to speed market familiarity and uptake
Public Relations Activities (media releases, etc.)	Increase general public's comfort level of nicotinic nomenclature particularly regarding the safety and lack of addictive potential for these drugs; may also generate excitement and pull-through demand
Market Research	Determine key drivers of pain prescribing, critical data points, entry niches, and compelling key messages

C.5.2 Communication Strategy [Andrea/Laura to review]

A comprehensive communication strategy for ABT-594 as a stand alone product and as the first product of the neuronal nicotinic receptor (NNR) class is in development. Due to the importance of the entire NNR program, a specialized communications strategy vendor (Ingenix) will be working with the internal ABT-594 team to craft the plan. The overall NNR program strategy will be focused on maximizing the market potential for ABT-594 and other compounds by:

- positioning these agents as novel, effective and safe

- generating awareness and educating prescribers and consumers about the NNR class and ABT-594 specifically
- establishing Abbott as the market leader in NNR science

Key to success of this strategy will be the cohesive, coordinated, and aligned efforts of R&D, commercial and public affairs. NUDR Discovery, the Analgesia Venture, NPD, AI NPP, and Public Affairs will work together with the vendor to lay out comprehensive Scientific, Marketing, and Public Relations plans that will outline communication timing, content, audience, and venue for all ABT-594 data. The primary goals of the communication strategy will be:

- position Abbott as the leader in NNR drug development
- augment internal development efforts
- build a base of supportive opinion leaders
- allay consumer concerns regarding the association of these compounds with nicotine
- build a framework for NNR product positioning
- generate market awareness for upcoming product launches

A complete communication strategy publication will be prepared during the third quarter of 2000.

- ~~The communications strategy for ABT-594 is under development. A vendor, specializing in the development and execution of communication strategies (e.g., Applied Clinical Communications) will be hired in 3Q, 2000 to develop the strategy, including proposed publications and venues for dissemination (e.g., journals and scientific meetings).~~

H.5 Patent Issues [Andrea/Jim S. to review] getting copy of patent to consider if we need to explore expanding its scope.

A notice of allowance has been obtained from the United States Patent and Trademark Office on an application providing generic coverage for ABT-594 and a large class of structurally related analogs. The original filing date for this application dates back to October 9, 1992, and since this predates a 1996 change in patent law, we are afforded a choice of 20 years from date of filing or 17 years from date of issue, of which 17 years from issue provides the longer patent life. The anticipated expiration of patent coverage for composition of matter for ABT-594 will be June, 2016. An additional application (6013.US.01), which includes species claims to ABT-594 as well as use claims for the treatment of pain, was filed in December, 1996 and is pending. If this patent is allowed, it will provide 20 years from date of filing, which will extend the patent life of ABT-594 to December, 2016.

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The original application providing generic composition of matter coverage was filed broadly ex. U.S. (WO94/08992) and this application published on April 28, 1994. A second foreign filing (WO96/40682) published on December 19, 1996. These cases are all still pending.

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Addenda

1.1 Highlights re: ABT-594

1.2 Historical Changes to ABT-594 Target Product Profile

- At PPCC, indications considered for ABT-594 were acute vs. chronic pain, with an acute pain claim being considered to have a shorter development course (if long term toxicology studies were not required).
- The FDA (3/98) related their concern that an oral dosage form may be used for chronic therapy even if labeled for acute. Long term toxicology would be required, therefore, even for acute claims.
- Decision analysis review of the program (3/98 - 7/98) arrived at several conclusions:
 - A general pain indication associated with a longer development cycle had greater value than an acute indication associated with a shorter development cycle.
 - Carcinogenicity studies should be initiated prior to first Phase II results.
 - Follow-on compounds (in the same cholinergic channel modulator class and in different pharmacologic classes) should be developed.
- Data from the first Phase II study (single dose molar extraction) indicated that ABT-594's onset of action is 1.5 - 2 hours post dose. Because a general pain indication requires efficacy in acute pain states (with more rapid onset of action), ABT-594 was considered unlikely to achieve a general indication. The current clinical plan targets disease-specific chronic pain indications.

The global target indications for ABT-594 are for the treatment of pain associated with diabetic neuropathy and for the treatment of pain with osteoarthritis.

Landsberg Deposition Exhibit 6

P's Exhibit CO



Laura Robinson
08/21/2000 12:07 PM

To: Andrea Landsberg/LAKE/PPD/ABBOTT@ABBOTT
cc: Michael K Biamesen/LAKE/PPRD/ABBOTT@ABBOTT, Bruce McCarthy/LAKE/PPRD/ABBOTT@ABBOTT
Subject: Re: ABT-594 Commercial Section w/ Laura Robinson Input

Thanks for the clarification Andrea...

Changing target profile for N&V to "low" probability should suffice, rather than changing the target itself.

I still think the COX-2s are too high a standard in terms of tolerability, at least based on Jim's and my original forecasting assumptions for the September 1999 Portfolio review, which set market share at 10% of PCN and 20% for NP.

I agree we cannot be too far behind current treatments in terms of tolerability, but our (J. Doran's and my assumptions for the September 1999 forecast used tramadol as the benchmark for AEs and efficacy in persistent chronic nociceptive pain, and gabapentin as the benchmark for efficacy in neuropathic pain (tramadol has 34% nausea, 31% dizziness, 23% somnolence and 13% vomiting; neurontin has 6% nausea, 27% dizziness, 31% somnolence and <5% vomiting).

The profile presented at the September portfolio review for PCN was "better efficacy than COX-2's/NSAIDS and tramadol with comparable AE's to tramadol (or better, with titration). For neuropathic pain, target efficacy was greater than gabapentin (AE profile for neuropathic pain vs nociceptive pain was not well defined, except to say that with titration, AE's could be somewhat worse than gabapentin, assuming greater efficacy. Appropriate trade-off between N&V, dizziness, somnolence, etc. will be difficult to judge without market research)

The market share in nociceptive pain (target market is limited to "persistent chronic", which is only 9.4% of the chronic pain population (base on J. Doran's estimates), and assumes only 10% share of this PCN market) reflects the fact that we do not expect large uptake in the patient segment that will experience adequate pain relief from COX-2s. We target efficacy greater than COX-2s and, therefore, we are not held to the same AE profile.

Please let me know if your assumptions have changed vs. the J. Doran's original (September 1999) forecast - your total sales numbers do look somewhat higher (\$367MM in 2008 vs current \$446MM), although your share assumptions are the same. Otherwise, I think the profile assumptions outlined under the forecast section should reflect the assumptions presented in the last Portfolio Review (efficacy superior to COX-2's/NSAIDS and tramadol in chronic nociceptive and superior to gabapentin in neuropathic pain; AE profile comparable to tramadol (or better with titration)

We can continue to discuss before final draft is due

Best Regards,

Laura

Laura

Andrea Landsberg



Andrea Landsberg

08/21/2000 10:56 AM

Landsberg DEP. EX. NO. 6
FOR ID., AS OF 2-16-07 BC

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To: Michael K Biarneser/LAKE/PPRD/ABBOTT@ABBOTT, Bruce McCarthy/LAKE/PPRD/ABBOTT@ABBOTT, Laura Robinson/LAKE/AI/ABBOTT@ABBOTT
 cc:
 Subject: Re: ABT-594 Commercial Section w/ Laura Robinson Input

Review of Laura's edits:
 No issues, of course, with any of the ex-us data or verbiage.

Positioning options - okay to change (Laura - I was taking comparable tolerability to not be applying just to N&V)

Target profile -- we changed the 'probability' for low N&V to LOW; I assumed we were trying to keep the 'history' of these changes so left as is -- if it is typical that we change these targets to reflect higher probability outcomes, it is fine with me to change.

Target product label -- I agree we are likely not to achieve such levels, however we need to be 'targeting' keeping these as low as possible via titration/ alternate formulations/ etc. These numbers were not meant to be 'absolutes' from me, just starting points for us to keep in mind vis-a-vis the competition -- Aldona and I discussed last week.

Pricing/reimbursement -- okay to change

Forecast assumptions -- again, not taking tolerability and safety to only be applying just to V&N; was thinking of dizziness re: gabapentin; also, COX-2s do have a lot of nausea that may have persistent duration, perhaps unlike 594's which may be transient (related to increasing dose) -- I do think, at least in the US, unless we are targeting just current opioid-using, severe pain population we will have to be that far behind these products (gabapentin and cox2s) in tolerability to get any use (especially in 2004). I am using this here to be sure we stay very aware of just how important this issue of tolerability is to gain any market share. I also thought that we were assuming the current trial with titration was supposed to greatly reduce the N&V issue (please let me know if this is a misunderstanding on my part) -- I know we have some definite signs that that is likely not the case (re: early discontinuations), but should we be adjusting assumptions before we really have all the data analyzed?

Table C4.2 -- noticed that the title says US, not Ex-US forecast

That's all I had comments on -- please let me know what the consensus views are. Mike, will we have one final chance to review the entire document again so that Laura and I can be sure we are comfortable with it in all its nuances?

Thanks,
 Andrea

Michael K Biarneser

 Michael K Biarneser 08/21/2000 09:04 AM
 To: Catherine K Kacos/LAKE/PPRD/ABBOTT@ABBOTT
 cc: Andrea Landsberg/LAKE/PPD/ABBOTT@ABBOTT, Aldona T Matalonis/LAKE/PPRD/ABBOTT@ABBOTT, Bruce McCarthy/LAKE/PPRD/ABBOTT@ABBOTT, Laura Robinson/LAKE/AI/ABBOTT@ABBOTT
 Subject: ABT-594 Commercial Section w/ Laura Robinson Input

Cathy,

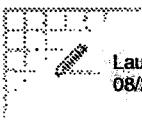
Attached is the commercial section with input from Laura (shown as edits in red.) I have also included some clarifications that Andrea and I agreed to. Please incorporate these changes into the controlled draft. Do not pick-up any edits to the draft label section without Aldona's input (Aldona - please review.)

Andrea / Bruce, Laura raises some questions in her input, most significantly the question in her cover note below. Please review and comment.

Mike B :



594 development plan - commercial sections, 8-21 with Laura Robinson & Mike E
----- Forwarded by Michael K Biarnesen/LAKE/PPRD/ABBOTT on 08/21/2000 09:00 AM



Laura Robinson
08/20/2000 06:27 PM

To: Michael K Biarnesen/LAKE/PPRD/ABBOTT@ABBOTT, Andrea
Landsberg/LAKE/PPD/ABBOTT@ABBOTT
cc:
Subject: Re: revised 594 development plan 

I was out of the office all last week at an Abbott off-site.

Attached are my edits. The only issue I have is that we still seem to be over-promising on the profile for ABT-594 regarding tolerability. There are several places where "tolerability comparable to COX-2's" is mentioned. I think this is completely out of the realm of possibility. What about changing it to "tolerability no worse than oxycontin" or maybe our target is better than that with titration, e.g, "comparable to gabapentin after titration". I don't believe that Jim Doran's any my original assumption for chronic nociceptive profile was "tolerability like COX-2s with high efficacy". I remember talking about tramadol as the benchmark, which still has fairly significant nausea/vomiting relative to typical NSAIDs.

What is your view on this?

Regards,

Laura

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B. Marketplace: Chronic Neuropathic and Nociceptive Pain

B.1 a Chronic Neuropathic Pain Marketplace SWOT Analysis

Table B.1a includes a summary of the strengths, weaknesses, opportunities and threats associated with the Chronic Neuropathic Pain marketplace with respect to the development of ABT-594.

Deleted: information presented in this section

Table B.1a SWOT Analysis (Strengths/Weaknesses/Opportunities/Threats)		
CATEGORY	ITEM (Impact)	STRATEGY
Strengths	<p>Indication in neuropathic pain will likely lead to spillover use in chronic nociceptive pain (High)</p> <p>Few products have indication for neuropathic pain, which should limit the sales and marketing efforts required to penetrate the market (High)</p> <p>Increasing incidence of diabetes and subsequent diabetic neuropathy market (Mod)</p> <p>Bulk of competition is generic (Mod)</p>	<p>Obtain indication for neuropathic pain (as broadly as possible)</p> <p>Conduct or fund trials in neuropathic and chronic nociceptive pain beyond diabetic neuropathy</p> <p>Capitalize on indication labeling through appropriate sales and marketing campaign</p>
Weaknesses	<p>Current leading treatment (gabapentin) perceived as effective, safe and well tolerated (High)</p> <p>Diabetic and other neuropathies are often underdiagnosed and mis/under-treated (Mod)</p> <p>Painful aspect of neuropathy is not always present or persistent (Mod)</p> <p>Limited regulatory history for indication (Mod)</p> <p>Advances in the treatment of glycemic control could decrease the rate at which diabetic neuropathy occurs (Low in near term)</p>	<p>Conduct trials to compare efficacy and tolerability to market leaders</p> <p>Monitor competitive landscape and adjust clinical development and marketing strategies appropriately</p> <p>Take advantage of cross-divisional expertise and presence in markets new to PPD (e.g.: Medisense in diabetes)</p> <p>Support screening and aggressive treatment of diabetic and other neuropathies</p> <p>Work closely with regulatory and plan for 'End of Phase II' FDA meeting</p>
Opportunities	<p>Large unmet need for effective treatments (High)</p> <p>Increasing focus on aggressive treatment of pain (Mod)</p> <p>Novel mechanism may generate increased excitement (Low)</p>	<p>Demonstrate equal or better efficacy to currently available agents</p> <p>Demonstrate equal or better tolerability to currently available agents</p>
Threats	<p>Gabapentin follow-on compound, pregabalin, may be even more effective than gabapentin and may pursue indication for neuropathic pain (High)</p> <p>Pricing pressure from managed care, government due to shift from low cost generics (Mod)</p> <p>Nicotinic association could decrease public acceptance and raise fears regarding addictive potential (Mod)</p> <p>Treatment aimed at the underlying neuropathic process (e.g. bimoclomol for diabetic neuropathy)</p>	<p>Maximize efficacy, safety and convenience of compound and formulation</p> <p>Conduct pharmacoeconomic studies and garner support of patient advocacy groups</p> <p>Develop and execute public relations plan to allay fears regarding nicotine</p> <p>Conduct studies to demonstrate non-addictive nature of compound</p>

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could limit market for neuropathic pain agent (Low)

B.1 b Chronic Nociceptive Pain Marketplace SWOT Analysis

Table B.1b includes a summary of the strengths, weaknesses, opportunities and threats associated with the ~~Chronic Nociceptive Pain marketplace~~ with respect to the development of ABT- 594.

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Table B.1b SWOT Analysis (Strengths/Weaknesses/Opportunities/Threats)

CATEGORY	ITEM (Impact)	STRATEGY
Strengths	Large, growing market consisting of primarily OA, RA and back pain (High) Increasing incidence of chronic pain conditions with aging population (Mod) Over 50% of chronic pain patients take a medication every day (Low)	Conduct trials in OA or other chronic nociceptive pain areas for indication or publication
Weaknesses	Titration may limit use relative to competitors (Mod)	Optimize titration schedule for least impact on prescribing and work on formulation to minimize or eliminate need for titration Consider addition of titration package for staff / samples
Opportunities	Significant unmet need for alternative to opioids that have equal efficacy with less side effects and no scheduling (High) "Ceiling effect" of NSAIDs and COX 2 competitors (Mod) Novel mechanism may generate significant degree of interest and trial (Mod)	Conduct opioid sparing or opioid replacement trials Conduct studies to demonstrate non-addictive nature of compound Position 594 as 'bridging' compound after ceiling effect reached and before use of scheduled narcotics
Threats	COX -2s may be firmly entrenched as market leaders for all chronic pain conditions (Mod) Combination products combining opioids with non-opioid analgesics or potentiators may meet market demand for improved side effect profile and offer steep competition (Mod)	Demonstrate key benefits over current and potential competitors in terms of efficacy or safety Carefully position along pain severity spectrum to preserve a target patient population

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B.2 Epidemiology/Disease Class

Pain is the most common symptom of disease and the most frequent complaint with which patients present to physicians. Chronic pain, including both neuropathic and nociceptive pain, is considered to be the single most common cause of suffering and disability in the industrialized

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world with an estimated 25-30% of the population experiencing some form of chronic pain. Chronic neuropathic pain is a frequent sequela of diabetes, cancer, AIDS and other viral infections, as well as 'entrapment' disorders such as carpal tunnel syndrome.

Diabetes and its major cause, obesity, are increasing at an alarming rate in the United States; the number of type II diabetics is estimated at 15 million in 2000. Despite advances in treatment, the development of diabetic complications such as neuropathy remains significant. The diagnosed prevalence of diabetic neuropathy is estimated to be about 2 to 3 million patients, with at least 10 to 20% of those patients experiencing painful symptoms.

It is estimated that almost a million people in the U.S. and 35 million people world-wide are infected with the AIDS virus. AIDS related neuropathic pain is estimated to affect approximately 40% of HIV-infected individuals. The primary form is a distal, symmetric, predominantly sensory neuropathy. A 1996 study found that only 15% of patients with AIDS related pain receive adequate treatment for their pain, with 25% receiving no analgesics and 40% being prescribed only NSAIDs indicating a significant unmet need for analgesia in this population. Post-herpetic neuralgia is another virally induced neuropathic pain syndrome. Annually, acute Herpes zoster infection (shingles) occurs in almost a quarter of a million people over the age of 60 in the US alone. Pain lasting more than one year has been reported in 22% of patients over the age of 55 and in 48% of those over 70 years of age. The incidence of acute shingles and subsequent post-herpetic neuralgia is likely to increase with the aging population.

In cancer, nerves can be damaged by mechanical distortion from a tumor mass, chemotherapy, or radiation therapy and therefore neuropathic pain is common. A 1999 report showed that 36% of cancer patients suffer from neuropathic pain and it is estimated that in half of cancer patients whose pain is rated as moderate or greater that primarily a neuropathic, rather than nociceptive, pain process is the cause. An estimate of the prevalence rate for cancer-related neuropathic pain in the US is 200,000.

Other neuropathic pain syndromes include entrapment neuralgias such as carpal tunnel syndrome (estimated 1% of the population) and some chronic low back pain patients (up to 10% of all chronic back pain is thought to be neuropathic in origin). Additional etiologies of neuropathic pain include amputations, multiple sclerosis, reflex sympathetic dystrophy, stroke, and spinal cord injury.

Chronic nociceptive pain categories include osteoarthritis, chronic back and neck pain, rheumatoid arthritis, and cancer pain and these diagnoses are expected to become more prevalent as the population ages. Current overall prevalence for these disorders is staggering, over 200 million worldwide, and, although the diagnosed and treated populations are lower, improved treatment options and awareness have the potential to drive significant growth. Osteoarthritis (OA) is one of the most common nociceptive pain conditions treated by primary care physicians and three-fourths of OA sufferers surveyed indicate that the disease interferes with their daily activities. Chronic back and neck pain are also highly prevalent and represent an estimated 40% of a PCP's chronic pain patient population.

A summary of the prevalence of relevant chronic pain diagnoses is shown in Table B.2c.

Diagnosis	Est. 2000 Prevalence (MM)	
	U.S.	Ex-U.S. ³
Neuropathic Pain in Diabetic Neuropathy ¹	0.6	0.9
Postherpetic and Trigeminal Neuralgia ¹	0.5	0.7
Osteoarthritis ²	9.4	24.3
Chronic Low Back Pain ²	8.5	21.6
Rheumatoid Arthritis ²	1.9	2.9
Cancer Pain ²	1.0	1.2
Total for Key Pain Diagnoses	21.9	51.6

1. Decision Resources, 1999.
 2. Decision Resources, 1999 (Data presented reflects *diagnosed* prevalence)
 3. Germany, France, Italy, Spain, UK, and Japan.

B.3 Market Overview

The economic burden of pain in the United States is estimated to be \$100 billion a year in direct and indirect costs. Approximately 95 million Americans per year receive drug therapy for pain,

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which represents only about 50% of those who suffer from pain. Physician or patient concern about drug safety and side effect profiles, fear of addiction, the use of OTC therapies, or non-pharmacological treatments account for the 30-50% of patients who seek treatment for pain but are not prescribed an analgesic. Efforts to change this mindset, however, are likely to result in a greater percentage of sufferers receiving pharmacologic therapy. Pain specialists, advocacy groups and patients have campaigned ~~successfully~~ for more aggressive treatment of pain over the last decade. One trend toward acceptance of this ~~more aggressive treatment approach~~ is the 11% and 14% growth (1999 over 1998) for codeine/codeine combination agents and morphine prescriptions respectively. ~~US sales of narcotic analgesics have also increased significantly, with an annual growth rate of 14% from 1997 to 1998, in the US, the great success of the recently launched COX-2 analgesics, achieved by growing the market with minimal erosion of the NSAID class, speaks to the increasing consciousness regarding pain management and the high unmet need for drugs that are safer, yet maintain equivalent efficacy, than those currently available. It is expected that, as improved treatments become available and awareness of the long term benefits of adequate pain management becomes widespread, the pain market will grow considerably. US sales of the COX-2's have been much less spectacular (\$1.35MM in 1999), likely due to the significant price premium over traditional NSAIDs, in an era when government health systems are experiencing downward pricing pressure. New pain treatments will need to demonstrate significant improvements over currently available agents to ensure regulatory approval (particularly in Europe) and widespread usage by physicians, who are increasingly involved in cost containment measures.~~

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Chronic pain sufferers may account for as much as 20% of the adult population implying over 130 million adults in the seven major pharmaceutical markets suffer from chronic pain. It is estimated that only one-half of chronic pain patients obtain adequate pain relief. The chronic pain market can be segmented into two major groupings, neuropathic and nociceptive. Chronic neuropathic pain includes the pain associated with diabetic polyneuropathy, post-herpetic neuralgia, sciatica, entrapment neuropathies (such as carpal tunnel syndrome), phantom-limb syndrome, and others. Chronic nociceptive pain includes pain associated with osteoarthritis, rheumatoid arthritis, lumbar spine disease, cancer, and other causes. Neuropathic and nociceptive pain differ in symptoms, pathophysiology and treatments.

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Neuropathic pain is a ~~significant~~, yet largely untapped market. Estimates vary widely for the number of worldwide sufferers, from as low as 20 million to as high as 50 million or more. Estimates of the number of cases is limited by inadequate epidemiological studies. One report puts the total US prevalence of neuropathic pain at 4 million. Neuropathic pain is often treated

with tricyclic antidepressants (TCAs), anticonvulsants (e.g. gabapentin) and alpha adrenergic agonists; collectively, these drug classes are sometimes referred to as "adjuvant pain medications". An estimated 50% of drug uses for neuropathic pain conditions are for anti-epileptic agents, with the TCAs accounting for about 25% of uses. PCPs prescribe OTC analgesics or prescription NSAIDs for neuropathic pain more than other specialties, even though there is little evidence for their usefulness in for this condition.

US sales in 1999 for the key ~~non-antiseizure~~ neuropathic pain treatments, Neurontin, carbamazepine, and tricyclic antidepressants (TCAs), are estimated to be \$350 million. Neurontin sales account for the bulk of this, with an estimated 40% of this antiepileptic drug's sales being for neuropathic pain; Neurontin's 2000 sales are expected to reach \$1 billion with perhaps 50% of its uses being for neuropathic pain. This dollar market value likely underestimates this market's potential due to a number of factors. Only the anticonvulsant Tegretol (carbamazepine), which is off-patent, has a specific indication for neuropathic pain in the US (although Neurontin (gabapentin) recently received an indication in the UK for the treatment of neuropathic pain). Therefore there has been no funding from the pharmaceutical industry to improve diagnosis and treatment of neuropathic pain and drive market growth. Of even greater impact on total market sales, most of the agents used to treat this population, with this exception of Neurontin, are low cost, generic products.

~~Ex-U.S. sales of carbamazepine and Neurontin for treatment of neuropathic pain are estimated to be approximately \$140MM in 1999. Carbamazepine is still the treatment of choice ex-U.S. with sales of approximately \$90MM in neuropathic pain. Neurontin has achieved only \$32MM in sales for this pain segment, with a price approximately 3-4 times that of carbamazepine, suggesting a patient share of only 10-20%.~~

Significant unmet need remains in the treatment of neuropathic pain since few medications provide complete pain relief and most adjuvant medications have significant side effects. As the prevalence of the underlying disorders (diabetes, herpes zoster, etc) increases with the aging population and more effective and tolerable medications become available, the neuropathic pain market has the potential to experience significant growth. The following tables show the factored U.S. and ex-U.S. prescription and sales volume for key neuropathic pain therapies 1999.

Table B.3a. 1999 Key Neuropathic Pain Products, Estimated TRxs

Class	1999 U.S. TRx	U.S. TRx CAGR	1999 ex-U.S. TRx	ex-U.S. TRx
-------	---------------	---------------	------------------	-------------

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	(MM)	'97-'99	(MM)	CAGR '97-'99
Neurontin	3.3	26.3%	N/A	N/A
Carbamazepine	1.0	12.6%	N/A	N/A
TCAs	8.2	1.1%	N/A	N/A
TOTAL	12.5	5.6%	N/A	N/A

Source: IMS, factored for neuropathic uses.

N/A = not available

Table B.3b. 1999 Key Neuropathic Pain Products, Estimated \$ Sales

Class	1999 U.S. Sales (\$MM)	U.S. Sales CAGR '97-'99	1999 ex-U.S. Sales (\$MM)	ex-U.S. Sales CAGR '97-'99
Neurontin	\$308	28.7%	\$53	37.9%
Carbamazepine	\$17	13.1%	\$81	2.5%
TCAs	\$26	-3.3%	NA	NA
TOTAL	\$351	21.7%	\$134	16.1%

Source: IMS, factored for neuropathic uses

Ex-U.S. data includes retail pharmacy data from all audited markets.

Deleted: and hospital data from major European markets and Canada only.

Nociceptive pain is categorized by duration (acute or chronic) and by severity (mild, moderate, and severe). The mild and, to a lesser extent, moderate segments have multiple product entries and are generally well satisfied by OTC products such as aspirin, acetaminophen, ibuprofen. The prescription market for nociceptive pain is made up of four key classes of analgesics: NSAIDs, COX-2s, Opioids (and combination products), and Other Non-Opioids (including aspirin, acetaminophen, and synthetic non-opioids).

Prescription NSAIDs are generally written for chronic pain of moderate severity. NSAIDs/COX-2s exhibit analgesic and mild anti-inflammatory properties, and are drugs-of-choice in such pain conditions as osteoarthritis, rheumatoid arthritis and lower back pain. NSAIDs/COX-2s have fewer central nervous system side effects than opioids. NSAIDs, however, can cause potentially serious renal and gastrointestinal side effects, including gastric ulceration and bleeding. COX-2s may appear to have a lower rate of these adverse events, due to increased selectivity of action. However, current COX-2s do not eliminate the risk of GI complications completely. Another drawback of NSAIDs/COX-2s is the presence of a 'ceiling effect' in which even additional amounts of drug fail to increase analgesic activity. This factor often leads to the use of stronger analgesics such as opioids.

The moderate and severe segments of the market have many opioid product offerings that are mostly generic, undifferentiated and inexpensive. While opioids and combination opioids accounted for the majority (53%) of analgesic prescriptions in 1999, they account for less than one-third of the prescription analgesic sales. Some branded opioids, however, have recently been very successful (OxyContin is projected to have 2000 revenues of \$1 billion).

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Opioids are scheduled, a regulatory status that creates administrative burdens and barriers to prescribing and these barriers are particularly high in European markets. In general, opioid use ex-US is largely restricted to cancer pain and there exists a large unmet need for effective treatment of severe pain. There are significant country to country differences, however.

Physicians in Scandinavia, the UK, and France are more likely to prescribe opioids compared to other ex-U.S. countries and use has increased considerably over the past 5 years. In Italy, Spain and Germany, opioid use is extremely restricted, requiring patient identity cards and special prescription forms that must be obtained, in person, by the physician; morphine is often considered a last resort.

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In the U.S., opioid analgesics are considered the drugs-of-choice for acute nociceptive pain, especially of moderately-severe to severe intensity. However, as elsewhere, US physicians often avoid prescribing opioids for chronic pain conditions due to fear of tolerance and addiction and due to the scheduled status of this analgesic class. As mentioned previously, the efforts of advocacy groups and pain specialists are being directed at encouraging appropriate use of strong pain medications and opioids are the most commonly prescribed medication for cancer pain.

“Other Non-Opioids” include (1) non-opioid/non-NSAID agents like aspirin, acetaminophen or Ultram (tramadol), and (2) NSAIDs that are positioned and marketed primarily as analgesics, such as ketorolac or bromfenac sodium. These non-opioids are generally used in place of opioids to treat moderate pain, or in some cases, moderately-severe pain.

Most analgesics are indicated for the treatment of one or more specific nociceptive pain states (e.g. osteoarthritis). Depending on its characteristics, however, a significant number of a product’s prescriptions may come from non-indicated pain states (i.e., spillover prescriptions). A product indicated for osteoarthritis, for example, is likely to be prescribed for chronic lower back pain, rheumatoid arthritis, and other pain states with similar clinical characteristics or etiologies. Efficacy in osteoarthritis has become a benchmark for analgesic efficacy in most chronic nociceptive pain states of mild to moderately severe intensity.

The following tables show U.S. and ex-U.S. prescription and sales volume for key nociceptive pain classes for 1999. Please note that up to 50% of these prescriptions may be for acute uses; also, not all chronic pain patients take medication every day and therefore also fall out of the potential population for ABT-594 treatment (due to its likely titration requirements).

Table B.3c. 1999 Key Prescription Nociceptive Pain Products, TRxs

Class	1999 U.S. TRx (MM)	U.S. TRx CAGR '97-'99	1999 Ex-U.S. TRx (MM)	Ex-U.S. TRx CAGR '97-'99
NSAIDs	70.7	-1.4%	N/A	N/A
COX-2s	22.4	N/A	N/A	N/A
Opioids ¹	153.8	2.5%	N/A	N/A
Other Non-Opioids ²	45.4	-0.9%	N/A	N/A
TOTAL	292.3	0.8%	N/A	N/A

Source: IMS

N/A = not available or not applicable

¹Includes IMS groups: Morphine, codeine and combos, propoxyphene, synthetic narcotics (non-injectables only)²Includes IMS groups: Synthetic non-narcotics, aspirin, acetaminophen (non-injectables only)

Table B.3d. 1999 Key Prescription Nociceptive Pain Products, \$ Sales

Class	1999 U.S. Sales (\$MM)	U.S. Sales CAGR '97-'99	1999 ex-U.S. Sales (\$MM)	ex-U.S. Sales CAGR '97-'99
NSAIDs	\$1,565	-3.2%	\$3,487	-0.5%
COX-2s	\$1,558	N/A	\$135	N/A
Opioids ¹	\$2,127	8.2%	\$767	14.2%
Other Non-Opioids ²	\$1,431	-4.6%	\$1,537	-0.6%
TOTAL	\$6,681	4.5%	\$5,661	1.1%

Source: IMS

¹Includes IMS groups: Morphine, codeine and combos, propoxyphene, synthetic narcotics (non-injectables only)

²Includes IMS groups: Synthetic non-narcotics, aspirin, acetaminophen (non-injectables only)

Ex-U.S. data includes retail pharmacy data from all audited markets.

Deleted: and hospital data from major European markets and Canada only.

B.4 Current Treatment Options

TABLE B.4A CURRENT ORAL TREATMENT OPTIONS: NEUROPATHIC PAIN

Category	Drug Class	Mechanism of Action	Pain Treated	Issues
Antiepileptics as analgesics*	Gabapentinoids (gabapentin)	Unknown	Distal symmetric neuropathic pain (diabetes, HIV, idiopathic, etc.) Post herpetic neuralgia (PHN)	Strength: Effective, well tolerated, not metabolized, no drug interactions Side effects: Dizziness at high doses Other drawbacks: No neuropathic claim in US; cost; modest analgesic effect, titration
	Iminostilbenes (carbamazepine)	Slows voltage-gated Na^+ channel activation recovery	Trigeminal neuralgia	Strength: Very effective, inexpensive Side effects: Ataxia, dysmetria, unsteadiness, hepatotoxicity, aplastic anemia, hypersensitivity reactions Other drawbacks: Drug interactions
Antidepressants as analgesics	Tricyclic antidepressants (amitriptyline, nortriptyline)	Probably inhibit biogenic amine reuptake	Distal symmetric neuropathic pain (diabetes, HIV, idiopathic, etc.) Post herpetic neuralgia (PHN)	Strength: Modest analgesic effect, inexpensive Side effects: Anti-cholinergic (dry mouth, sedation), cardiac arrhythmia, weight gain Other drawbacks: Cardiac effects, titration
	Mixed serotonin and norepinephrine reuptake inhibitors (venlafaxine)	Mixed serotonin and norepinephrine reuptake inhibitors (venlafaxine)	Distal symmetric neuropathic pain (diabetes, HIV, idiopathic, etc.) Post herpetic neuralgia (PHN)	Strength: Modest analgesic effect, inexpensive? Side effects: Anti-cholinergic (dry mouth, sedation), cardiac arrhythmia Other drawbacks: Cardiac effects, titration
Miscellaneous	Opioid and norepinephrine reuptake inhibitor (tramadol)	Opioid and norepinephrine reuptake inhibitor	Distal symmetric neuropathic pain (diabetes, HIV, idiopathic, etc.) Post herpetic neuralgia (PHN)	Strength: Moderate pain relief without the opiate stigma, non-scheduled Side effects: Nausea, vomiting, sedation Other drawbacks: May reinitiate physical dependence in previously opioid-dependent patients. May eventually receive scheduled status

* Many newer antiepileptic agents (e.g., Tiagabine, lamotrigine) have recently or will soon undergo clinical trials in neuropathic pain.

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TABLE B.4B CURRENT TREATMENT OPTIONS: NOCICEPTIVE PAIN

Category	Drug Class	Mechanism of Action	Pain Treated	Issues
Opioid	Opioids (e.g., morphine, cocaine)	Opioid receptor activation	Surgery, injuries, musculoskeletal disorders, cancer Moderate to severe pain Opioids are the drugs of choice for severe acute pain and cancer pain	Strength: Potent analgesic effect, inexpensive Side effects: Constipation, Nausea and Vomiting, Sedation, Cognitive Impairment, Respiratory Depression, Pruritis Other drawbacks: Development of tolerance, addiction potential, scheduled drugs, do not reduce inflammation
	Opioid Combination with another analgesic (e.g., aspirin or acetaminophen)	Opioid receptor activation Combination preparation offsets opioid side effects by adding second analgesic with a different mechanism of action	Surgery, injuries, musculoskeletal disorders Moderate to severe pain	Strength: Potent analgesic effect, and depending on combination agent, may also decrease inflammation and body temperature; reduced opioid side effects Side effects: All effects associated with each of the drugs administered, although reduced in frequency and severity Other drawbacks: All drawbacks associated with each of the drugs administered
Non-Opioid	NSAIDS	Inhibit the synthesis of prostaglandins, which are responsible for inflammation, increased body temperature, and sensitization of pain receptors	Osteoarthritis, rheumatoid arthritis, lower back pain, and other chronic pain conditions in addition to some mild to moderate acute pain conditions	Strength: Fewer CNS side effects than opioids, and no addiction potential, inexpensive Side effects: Gastric ulceration and bleeding Other drawbacks: Ceiling effect (complete pain relief cannot be achieved even after dose escalation)

TABLE B.4B CURRENT TREATMENT OPTIONS: NOCICEPTIVE PAIN (CONT.)

Category	Drug Class	Mechanism of Action	Pain Treated	Issues
Non-Opioid (con't)	COX-2 Inhibitors (e.g., celecoxib)	Inhibit the synthesis of prostaglandins, which are responsible for inflammation, increased body temperature, and sensitization of pain receptor Preferential COX-2 vs. COX-1 inhibition may reduce risk of GI interaction	Osteoarthritis, rheumatoid arthritis, lower back pain, and other chronic pain conditions in addition to some mild to moderate acute pain conditions	<u>Strengths:</u> Claim fewer GI side effects than NSAIDS with similar analgesic effect <u>Side effects:</u> Peripheral edema <u>Other drawbacks:</u> cost
	Acetaminophen	Mechanism of action is poorly understood, but appears to involve effects in the CNS (has analgesic and antipyretic effects)	Sprains, strains, injuries, musculoskeletal pain, osteoarthritis Management of mild to moderate pain	<u>Strengths:</u> Has no effects on platelet function, has no GI toxicity; has fewer CNS side effects than do opioids, inexpensive <u>Side effects:</u> May be hepatotoxic in heavy drinkers and patients with liver disease <u>Other drawbacks:</u> Lacks anti-inflammatory activity. Ceiling effect (complete pain relief cannot be achieved even after dose escalation)
Miscellaneous	Opioid and norepinephrine reuptake inhibitor (tramadol)	Dual mechanism of action via opioid and non-opioid mechanisms (norepinephrine reuptake inhibitor)	Used in the treatment of moderate to severe pain	<u>Strengths:</u> Moderate pain relief without the opiate stigma, non-scheduled <u>Side effects:</u> Nausea, vomiting, sedation <u>Other drawbacks:</u> May reinitiate physical dependence in previously opioid-dependent patients. May eventually receive scheduled status

B.5 Competitive Analysis – Emerging Competition [Andrea/Laura to review]

Almost 100 compounds are currently in development for prescription pain management, though some of these compounds are also being developed for other non-analgesic indications. The majority of the analgesic compounds in the pipeline represent incremental improvements to the opioids or NSAIDs, or consist of new formulations or delivery mechanisms for the standard analgesics. Fewer than 30% of the compounds in development have novel mechanisms of action. Drugs with novel mechanisms are expected to provide the bulk of the promoted competition for ABT-594.

Among the novel agents in development, the greatest threat to ABT-594 is likely to be posed by other nicotinic compounds in development for pain. ABT-594, now in Phase IIb trials, is suspected to be the most advanced nicotinic compound in the analgesia pipeline. The first nicotinic compounds from competitors to be launched in the class may be for Alzheimer's Disease or Parkinson's Disease. These compounds do not represent a threat to ABT-594, unless significant safety concerns or evidence of tolerance, dependence or abuse are an issue and become associated with the class as a whole.

The pipeline for the treatment of neuropathic pain does not have a blockbuster compound on the order of the COX-2 inhibitors. However, pregabalin, the follow-up to Parke-Davis' Neurontin (gabapentin), is expected to perform well; analyst reports predict its sales for neuropathic pain may be almost \$100 million by 2003, its second year post expected launch. Initial data from pregabalin suggests a compound that overcomes the absorption and uptake limitations associated with gabapentin leading to a more convenient dosing schedule and resolved pharmacokinetic 'ceiling effect'. However, increased doses and corresponding increased plasma levels appear to be associated with greater efficacy and more frequent adverse events. The marketing and sales power of Pfizer is likely to drive the product to success, despite such concerns.

For the treatment of osteoarthritis (OA), the COX-2 inhibitors represent the most significant competition, with sales of a staggering \$13 billion by 2004 being predicted. Use beyond pain into colorectal cancer and neurodegenerative disorders is also being explored for COX-2s. Searle and Merck both have follow-up compounds well along in development which purport to have greater selectivity for COX-2 vs. COX-1 and therefore offer the potential for increased potency and decreased side effects. Other second generation COX-2s are in the pipeline, although J&J recently announced the decision to stop development of Japan Tobacco's compound JTE 522. Unresolved side effect issues surrounding COX-2 inhibitors remain, however, including the risks

of thrombosis, hypertension, reproductive dysfunction and teratogenicity that may show up as the exposure to these agents becomes more widespread.

Table B.5a. Analgesia Pipeline – Key Novel Agents

Product	Company	Mechanism	Phase	Comment
pregabalin	Parke-Davis	Ca channel blocker	III	Neuropathic pain, chronic pain Follow-up to Neurontin
saredutant	Sanofi	NK-2 receptor antagonist	II	General pain MOA losing favor; active program?
ZD4952	Zeneca	prostaglandin receptor antagonist	II	Moderate to severe pain
GV196771	Giloxo	glycine antagonist	II	Chronic pain, showing promise
tepoxalin	J&J	COX/5-LO inhibitor	II	OA, described as 'steroid replacing anti-inflammatory drug'
darbufelone	Parke-Davis	COX/5-LO inhibitor	II	General pain
HCT-3012	NicOx	Nitric oxide NSAID	I	Pain and inflammation
cizolirtine	Esteva	Substance P	II	Analgesia, antipyretic

Sources: ADIS, IMS, Decision Resources, company reports

Table B.5b. Development Pipeline – Nicotinic Mechanisms

Product	Company	Phase	Comment
GTS-21	Taiho	II	Target is Alzheimer's Disease May have preclinical pain program; looking for partner
CMI 980	Cytomed	Preclinical	Target is pain Epibatidine analog
SIB-T1887	Sibia	Preclinical	Target is pain
FID 072021	Fidia	Preclinical	Target is pain; not actively funding

Sources: ADIS, IMS, company reports

Not reflected in the above tables are the early stage programs of Merck, Sibia, etc..(Bruce to complete).....

B.6 Unmet Needs [Andrea/Laura to review]

In general, a significant unmet need exists for safer, non-abusable, non-addicting, non-tolerance producing, and non-scheduled efficacious oral and parenteral analgesic products for the treatment of moderate to severe neuropathic and chronic nociceptive pain.

Table B.6. Unmet Market Needs and the Impact of the Pipeline

Unmet Need	Pipeline Impact
Efficacy in moderate to severe pain without tolerance, dependence or abuse	Novel nicotinic agents like ABT-594 may provide efficacy in more severe pain states without opioid-like liabilities
Efficacy in neuropathic pain	Pregabalin may provide incremental improvement in neuropathic pain efficacy over gabapentin, but may also have increased frequency of adverse events Novel nicotinic agents like ABT-594 appear to have efficacy in neuropathic pain, based on animal models
Reduction in the GI bleeding risk of NSAIDs	COX-2 inhibitors appear to reduce the incidence and severity of GI ulcers and bleeding; second generation COX-2s may increase therapeutic window further
Overcome ceiling effect of NSAIDs	Preclinical studies did not indicate a ceiling effect for novel nicotinic agents like ABT-594
Extended dosage intervals or novel delivery mechanisms for improved compliance and convenience	Once weekly dosing formulations being explored for COX-2s, etc. Patch technology improvements likely
Therapies aimed at disease modification, prevention	Agents that decrease rate of diabetic complications (e.g., aldose reductase inhibitors) or directly treat neuropathy (bimoclomol) may decrease incidence of neuropathic pain

C. Product Positioning

C.1 Product Positioning Options

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Table C.1a includes a summary of the strengths, weaknesses, opportunities and threats associated with the information presented in this section with respect to the development of ABT-594.

Positioning alternatives/options	Strategy	Strengths	Weaknesses
Equal efficacy to Neurontin and TCAs in neuropathic pain with improved dosing, AEs, and safety	Sell against top neuropathic pain products on convenience, tolerability and safety	Efficacy to date supports BID, possibly QD dosing Low level of CNS AEs No weight gain	May have too high level of nausea and vomiting to compete with Neurontin (pregabalin?) on AEs
Better efficacy than Neurontin and TCAs with comparable dosing, AEs and safety	If AEs for ABT-594 too frequent vs. competition, sell on 'power'	Efficacy data likely to support May be better fit with AE profile	Neurontin and TCAs <i>perceived</i> to have high efficacy; may not be able to match Neurontin's perception as extremely safe and well tolerated
The only oral agent indicated for the treatment of neuropathic pain	Capitalize on 'government approved' status to increase prescriber confidence	Data to date supports efficacy in neuropathic pain Current timeline gives ABT-594 neuropathic pain indication by mid 2004	Pregabalin (or others?) may be to market first with neuropathic pain indication Neuropathic pain indication still uncertain from regulatory standpoint
Superior efficacy to COX-2s without ceiling effect (or if I don't think "comparable tolerability" in COX-2s is even a realistic possibility, we will be forced to have comparable tolerability to marketed COX-2s)	Market "chronic neuropathic" patients targeting patients who receive insufficient pain relief from COX-2s	No ceiling effect seen with ABT-594	May limit use to <i>after</i> COX-2 failure COX-2 agents will be firmly entrenched
Opioid-like efficacy without addictive potential and with fewer AEs than opioids for treatment of moderate to severe chronic pain	Capitalize on market reluctance to use opioids by providing safe, efficacious alternative	Provides clear, compelling reason to use and matches product profile to date	May niche ABT-594 to more severe patients and limit market

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C.2 Target Product Profile

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C.2.1 ABT-594 Target Product Profile

Table C.2.1 below, outlines the desired target product profile for ABT-594:

Table C.2.1. ABT-594 Target Profile

PPCC/DDC Profile (12/10/97)	Current Profile (8/00)	Rationale for Profile Change	Probability	Status	Share Impact
Indicated for the treatment of pain (general pain claim)	Indicated for the treatment of osteoarthritis pain	"General pain" claim not achievable due to slow onset of action; proof of principle established in molar extraction study Indication specific claims now favored since general pain claim not achievable, since acute, chronic, nociceptive pain matter	Medium	9/99, 1Q01	High
Effective in neuropathic pain	Indicated for the treatment of neuropathic pain	Indication specific claims now favored since general pain claim not achievable	Med	9/99, 2Q01	Medium
Effective for moderate to moderately-severe pain	N/A	No longer applicable without general pain, acute or chronic pain (not otherwise specified) claims??	N/A	N/A	N/A
Not scheduled/no abuse potential?	No change	N/A	High	4Q02	High
Improved safety profile compared to opioids including: - less GI motility impairment - less respiratory depression - low tolerance potential - no dependence/withdrawal	No clinically significant tolerance, dependence or withdrawal In contrast to opioids, no constipation or respiratory depression liability Tolerability comparable to currently used neuropathic and chronic nociceptive pain products	Simplify profile to focus on the most commercially important AEs Need to be well-tolerated to sell in crowded market with many alternatives	Medium	2Q01	High
	Very few abnormal LFTs	Abnormal LFTs in a few Phase I subjects	High	9/99	High
	Very low nausea/vomiting at effective dose at this medications should we change to. Comparable to mild sedative, e.g.	Incidence of nausea/vomiting in single dose Phase I & II subjects (food and dose dependent) similar to opioids	Low	9/99	High

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	expressing a \$2 billion CRM to fund we cannot afford to do this product						Deleted: [redacted]
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Table C.2.1. ABT-594 Target Profile (cont.)

PPCC/DDC Profile (12/10/97)	Current Profile (8/00)	Rationale for Profile Change	Probability	Status	Share Impact
	Other safety OK	Simplify profile	Medium	9/99, 2Q01	High
	No significant or sustained differential efficacy in nicotine users vs. non-nicotine users	No difference seen in efficacy to date	High	9/99, 2Q01	Med
	No restrictions for use in nicotine users	Lower incidence of AEs in nicotine users in Phase II trial	High	9/99, 2Q01	Medium
	No re-initiation of cravings in ex-nicotine users	Possible due to nicotinic mechanism	Medium	2Q01	High
Onset of action in less than 30 minutes	Onset of action at 1.5 to 2 hours	Onset of action estimated at 90 minutes in Phase II trial	Low	9/99	Medium
BID/TID dosing	BID/QD dosing	Competitive dynamics highlight importance of dosing convenience	High	9/99	Medium
No major drug interactions, especially with drugs used for common chronic conditions	No change	N/A	High	4Q00	Medium

C.2.2 Target Product Label Bruce: not sure if I was supposed to do this but thought I'd add some key points – I'd like to review in its entirety when technical sections completed, if I may.

Label Requirement	Desired Label claim/ Minimally Acceptable Criteria for a Commercially Viable Product/Competitive Advantage	Regulatory Requirements	Studies/Activities/Other strategy to Achieve
DESCRIPTION			
Formulation	odorless, tasteless, tablet or capsule – small, easy to swallow, marketable color!		
Dose form			
Dose strength(s)			
Route of Administration	oral (or patch?) is oral suspension a possibility? – something to consider for elderly population...		
CLINICAL PHARMACOLOGY			
MECHANISM OF ACTION (MUST INCLUDE)	acts on neuronal nicotinic receptors, a subset of cholinergic receptors.... (then something pharmacologic to substantiate lack of addictive quality if possible)		
Pharmacodynamics			
Pharmacokinetics	if favorable (i.e: if we are similar to Celebrex) include table like table 1 in Celebrex PI)		
Absorption/Bioavailability			
Distribution			
Protein binding			
Distribution			
Metabolism			
Elimination			
Special Populations			
Effect of age	ideally none, downward dose adjustment in elderly okay		
Effect of gender	none		
Effect of race	none		
Use in pregnant women	preg category c (no worse!)		
Use in Nursing Mothers			
Effect of concomitant disease	ideally none		

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Plasma Levels and clinical effect	best not to elucidate unless necessary		
Effect of food on absorption	very ideally NONE.		
Clinical Trial Data (by indication)	Neuropathic pain: ABT-594 has demonstrated significant reduction in neuropathic pain (+/- time to onset of relief if positive) (diabetic neuropathy? and others?) as demonstrated by changes in Likert pain scale. list any secondary measures (other pain scales, such as subjective scores, effect on daily activity, wellbeing, and other QOL measures (SF36 or others), ?mobility measures?). Any chance of 'stiffness' or ??strength improvements? (even if not direct....)		
Phase 3 studies	"Special Studies": gastrointestinal monitoring - endoscopic tracking vs. ibuprofen		
INDICATIONS AND USAGE	Indicated for the treatment/relief? of neuropathic pain (associated with diabetic neuropathy (alone or with others?)) Potentially OA?		
Clinical Trial Data (only for one indication, the rest in C.P.)			
CONTRAINdications			
CONTRAINDICATIONS			
WARNINGS			
Black box warnings	NONE		
General Warnings (e.g., thrombocytopenia)	None?		
Usage in Pregnancy	not important		
PRECAUTIONS			
General			
Information for Patients			
Lab Tests			
Drug Interactions	NO CLINICALLY SIGNIFICANT INTERACTIONS with common diabetes drugs, psychotropic drugs, antihypertensives, anticholesterol/lipid lowering agents, NSAIDs, COX-2s, aspirin		
Drug/Lab Test Interactions	NONE with HbA1c.		
Carcinogenesis			
Mutagenesis			
Impairment of Fertility			
Pregnancy			
Nursing Mothers			
Pediatric			
Geriatric			
ADVERSE REACTIONS			

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Controlled Phase III study data (by indication)	Nausea < 8%, dyspepsia <10%, vomiting <3%, abdominal pain <5%, diarrhea <5%, dizziness <3%, are the most frequently reported adverse reactions? weight gain <2%, fatigue <2%, somnolence <2%, ataxia <2%, tremor <2%, other CNS <2%, anti-cholinergic effects <2%		
Other patient populations			
OVERDOSAGE			
OVERDOSAGE			
DOSAGE AND ADMINISTRATION			
By indication (dose/levels/length of treatment)			
Monitoring of Patients			
General dosing advice			
HOW SUPPLIED			
HOW SUPPLIED			

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C.2.3 Desired Promotional Claims

Table C.2.2 below, outlines the minimally acceptable criteria for a commercially viable product for ABT-594. Items in shaded boxes are NOT FUNDED.

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C.2.2 Desired key messages should follow:

Desired key message	Provenatory information	Measures	Timing	Study duration	Type of message	Probability	Share Impact	Comments/Risks
Significantly reduces pain associated with diabetic neuropathy	At least 2 adequate, well controlled studies	11 point Likert pain intensity	Launch	Phase III studies (TBD)	Efficacy	Medium	High	
Efficiency and tolerability comparable to Neurontin and/or Trileptal in neuropathic pain	At least 1 adequate, well controlled comparator study	Appropriate pain scale, Out/come scale (HEDS if available)	Within 3 years of launch	Phase IV (TBD)	Efficacy, tolerability, patient satisfaction	Low	High	High risk but may be necessary to capture significant share especially if competitors indicated. Difficult to conduct as competitor not interested
Significantly reduces pain associated with osteoarthritis	At least 2 adequate, well controlled studies	WOMAC, 4-point categorical pain intensity	Launch or ASAP if launch within 1 year neuropathic pain indication	Phase III studies (TBD)	Efficacy	Medium	High	
Efficiency and tolerability comparable to COX-2s and/or Rivaroxaban in DAs	At least 1 adequate, well controlled comparator study	Appropriate pain scale, Out/come scale (HEDS if available)	Within 3 years of launch	Phase IV (TBD)	Efficacy, tolerability, patient satisfaction	Low	High	High risk but may be necessary to capture any share
No clinically significant tolerance, dependence or withdrawal	Phase II/III trial; specialized addiction studies	AE reports, specific addiction measures	Launch	All studies	Safety	Medium	High	
Well tolerated in comparison to in combination with opioids, with no constipation or respiratory depression liability	Phase II/III trials	AE reports	Launch	All studies	Safety	Medium	High	

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Desired key message	Regulatory requirement	Measure	Timing	Study Number	Type of message	Probability	Share Impact	Comments/Risks
Competitive rate of nausea-and-vomiting given level of efficacy Well tolerated in comparison to commonly used pain medications	Phase I/II trials	AE reports and efficacy measures	Launch	All studies	Safety	Medium	High	
Easy to use with BID/QD dosing and minimal titration	Phase I/II trials, market research	Study protocols, patient surveys, MD market research	Launch	All studies	Convenience and compliance	High	High	
Cost effective	Phase III and IV	Pharmacoeconomic data	Launch or shortly thereafter	TBD	Cost	Medium	Medium	Important for MC formulary acceptance
Higher patient satisfaction than other comparable medications	Phase III and IV	Survey, QoL measures (HEDIS if available)	Launch or shortly thereafter	TBD	Satisfaction	Medium	Medium	
No clinically relevant drug interactions	Preclinical, Phase I, II, III trials	Clinical and pre-clinical measures?	Launch	All studies	Safety and convenience	Medium	Medium	
Safe for long term use	Phase III extension	AE reports	Following launch?	TBD	Safety	Medium	Medium	

¹HEDIS: Health Plan Employer Data and Information Set: developed by NCQA (National Committee for Quality Assurance) for Managed Care Organization accreditation.

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C.3 Pricing/Reimbursement Strategies

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C.3.1 Pricing Strategy [Andrea/Laura to complete]

a. U.S.

The Pain Market's overall pricing in the U.S. market will remain relatively stable in the short term due to two factors. First, the effect of higher-priced branded products entering the market in each analgesic class is tempered by the loss of patent protection of other branded products, and the resulting price erosion due to generic competition. Secondly, the large size of the prescription pain market, and the large number of product offerings in each class, tends to absorb the impact of individual products' prices.

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The tremendous success of the COX-2 launches in the US, with prices higher than their competition, demonstrate the low price elasticity of demand of the US pain market. Celebrex and Vioxx sell at a 50% premium over other branded anti-arthritis drugs and offer only modest gains in safety. In the neuropathic pain market, Neurontin, with costs per prescription similar to the COX-2s, is seeing continued growth despite the low cost, effective alternative offered by the TCAs. Here again, Neurontin is perceived as offering improvements in safety and tolerability over its generic competition. The unmet need for effective analgesics with improved safety profiles, coupled with the increasing sensitivity regarding aggressive pain treatment contribute to this market dynamic.

Pricing new, and particularly novel, products at a reasonable premium will likely continue to be the norm in the years leading up to the launch of ABT-594. Current forecast assumptions put the price of ABT-594 at a level comparable to Celebrex and Neurontin, grown at a modest 2%/year to launch year AWP of approximately \$95 for a 30 day prescription.

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b. Rest of World

Pricing for pain medications ex-US have traditionally been 50% of US prices. Both the COX-2's and gabapentin were introduced at significant price premiums relative to other pain medications. In the countries where the COX-2s have launched, they are priced approximately 20% higher than tramadol and approximately 100% higher than branded cold standards like naproxen and diclofenac. Penetration of the COX-2's has been rather limited thus far - only \$13MM in ex-US

markets. This is partially due to delayed launch relative to the US (COX-2s have not yet launched in Japan and many markets in Europe). It may also be due to significant price premiums, which physicians may not feel is justified for the relative modest increases in safety. Neurontin is priced at almost a 20% premium vs. the COX-2's (\$1.2 vs. \$1.0/day), but is comparably priced to the newer anti-seizure drugs. The relatively low penetration of Neurontin in either neuropathic pain or other uses (only \$105MM in ex-US retail pharmacy sales after 5 years on the market) may also be due to a low perceived improvement relative to less expensive gold standards.

New pain medications will need to demonstrate a true advantage in efficacy and/or side-effects to receive regulatory approval, especially by the IMPA; assuming the target efficacy and tolerability profile of ABT-594 is achieved, ABT-594 would achieve such an advantage. Because ABT-594 may have application in both neuropathic and chronic nociceptive pain, the ex-US pricing assumption for ABT-594 is comparable to COX-2 pricing. The current average price for COX-2's is approximately \$1.10 per day; however, this reflects a large percentage of sales in "free-pricing" countries which tend to have higher than average prices. Therefore, the average ex-US price is assumed to be approximately \$0.90/day.

C.3.2 Reimbursement/Managed Care

In 1999, 40% of anti-arthritis prescriptions were covered by managed care and 15% by Medicare/Medicaid. A significantly higher percentage, 35%, of COX-2 prescriptions were covered by the government plans, with managed care covering about 30% of the prescriptions for this class. The continued entry of higher-priced, novel analgesics may create some upward trend in prescription analgesic prices over the next 5 years; reaction from government and managed care payors to rising costs could then create pressure to contain costs. However, while managed care and the government will likely pay increasing attention to this market as costs rise, strong efforts to restrict coverage of safer, novel analgesic alternatives are difficult to imagine given the large portion of elderly and disabled in the pain population and the potential for serious backlash to such an unsympathetic stance.

As is now standard in the industry, some level of managed care organization (MCO) rebating for ABT-594 will be necessary. Rebating may be kept below 15% due ABT-594's novel mechanism of action and a potentially unique indication for neuropathic pain; significant discounting may be needed for deep penetration of the broader chronic pain market. The current forecast assumes fairly standard discounts of approximately 15% for managed care and 35% for Medicaid/Medicare.

Due to the competitiveness of the pain management market and the standard expectations of MCOs, ABT-594 must still favorably complete outcomes and pharmacoeconomic studies in order to gain significant formulary acceptance and use in MCOs and institutional settings. Marketing research and consultation with the PPD Managed Care department will help determine the appropriate number of studies, comparators and desired endpoints. Inclusion of these measures into Phase III trials is key for the early acceptance and success of this product.

Table C.3.1. Pricing/Reimbursement Strategies		
Pricing Strategies	Strategy to Achieve	Requirements/Status (i.e. met or unmet)
US		
<ul style="list-style-type: none"> Price at level comparable to COX-2s/Neurontin (leading, novel branded products in OA/RA and neuropathic pain markets respectively) 	<ul style="list-style-type: none"> Quality of life and pharmacoeconomics end points in Phase III studies Pharmacoeconomic model Head-to-head comparator trial demonstrating improved QOL, and/or cost savings First in class 	<ul style="list-style-type: none"> Unmet Unmet Unmet Unmet
Europe	<p>..... Same as for U.S. comparator trials will be essential for success required</p>	<ul style="list-style-type: none"> Unmet
Japan	<p>..... Same as for U.S.</p>	<ul style="list-style-type: none"> Unmet

C.4 Sales Forecast(s) for ABT-594

C.4.1 U.S. Sales Forecast

The U.S. sales forecast for the neuropathic and chronic persistent pain market is shown in Table C.4.1, below.

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Table C.4.1 U.S. Forecast (Date of Forecast: 7/00)					
	2004	2005	2006	2007	2008
Chronic Persistent Nociceptive (OA) Market Rxs (MM) - % chg	36.6 0.5%	36.8 0.5%	37.0 0.5%	37.2 0.5%	37.4 0.5%
Neuropathic Market Rxs (MM) - % chg	10.7 5%	11.3 5%	11.8 5%	12.4 5%	13.0 5%
Abbott Share CPN(%)	1%	3%	6%	8%	10%
Abbott Share NP(%)	4%	8%	12%	16%	20%
Abbott Rxs CPN(000)	328	1,051	2,220	2,976	3,738
Abbott Rxs NP(000)	427	903	1,418	1,986	2,606
Price/Rx (WAC) (2%/year increase)	\$77.60	\$79.15	\$80.70	\$82.30	\$84.00
Abbott Sales (\$MM)	\$53.1	\$140.1	\$246.4	\$342.6	\$446.9
R&D (\$MM)	\$18	\$8	\$3	\$3	\$3
SG&A (\$MM)	\$67.9	\$63.2	\$66.3	\$60.6	\$58.3
MM (%)	\$51.5	\$136.0	\$239.3	\$333.0	\$434.6
Div. Margin (\$MM)	(\$27.7)	\$66.6	\$168.7	\$267.1	\$370.0

10 year pre-tax NPV @ 12.5% = \$720 MM

10 year after-tax NPV @ 12.5% = \$427 MM

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Key forecast assumptions:

- NDA Filed 5/03, Launch 5/04
- First Neuronal Nicotinic Receptor compound for pain to market
- Indicated for treatment of neuropathic pain; significant publication, or indication, from large scale trial on use in some form of chronic persistent nociceptive pain (e.g.: OA) in 2006
- Efficacy equal to gabapentin, ibuprofen
- Good tolerability and safety profile; comparable to gabapentin, COX-2s ~~???~~ I don't think J. Ivercan's model assumed tolerability equal to COX-2's. Safety w/ tolerability no. "Very low nausea/vomiting at effective dose" is stated in the current profile, which should probably be changed to "nausea/vomiting no worse than mild opioids, ~~as execoin~~"
- No addictive potential
- Titration of 3-5 days
- Peak share 20% in neuropathic pain, 10% in chronic, persistent nociceptive pain (including off-label, 'spillover' prescriptions)
- Significant promotional and PR spend in early years
- Physician targets: D6-10 Neuros, D3-10 Rheumatologists/Endocrinologists, D9-10 PCPs
- Sampling at 80% of details at launch, 5 units per detail, 7 days of therapy per unit

- Cost comparable to Neurontin and Celebrex
- Significant payor discounting
- Stocking at 8% of first year's sales
- Patent expires 12/2016

Forecast Update Plan:

Forecast will be updated pending analysis of Phase IIb clinical trial results (March or April 2001) or before if the clinical trial plan changes from current assumptions. *in late June/early July 1999 to account for revised indications of OA and/or neuropathic pain and the associated spillover use in other pain states. Forecast will be available well in advance of ABT-594 Go/No-Go decision in 9/99.*

C.4.2 Ex-U.S. Sales Forecast

The Ex-U.S. sales forecast is shown in Table C.4.2, below.

Table C.4.2. U.S. Forecast (Date of Forecast: 8/99)					
	2004	2005	2006	2007	2008
Chronic Pain/Neuropathic (CPN) Rx _s (MM)		70.8 1.5%	71.0 1.5%	71.1 1.5%	71.1 1.5%
% chg					
Neuropathic/Migraine Rx _s (MM)		38.2 1%	43.6 1.5%	45.9 1.5%	47.1 1.5%
% chg					
Abbott Share CPN (%)	22	18	16	15	15
Abbott Share N/M (%)	59	83	129	169	169
Abbott Rx CPN (MM)	1,180	1,206	1,231	1,256	1,281
Abbott Rx N/M (MM)	1,208	1,253	1,327	1,402	1,482
Proctor & Gamble (P&G)	\$22.0	\$22.4	\$22.8	\$23.2	\$23.6
Abbott Sales (MM)	380	415	434	454	474
R&D (MM)	\$12	\$12	\$12	\$12	\$12
SG&A (MM)	\$28	\$28	\$28	\$28	\$28
SNMM (%)	97%	97%	97%	97%	97%
Div. Margin (MM)	(\$120)	(\$21)	\$41	\$105	\$188

10 year ex-tax N/P @ 12.5% = \$322 MM
10 year after-tax N/P @ 12.7% = \$187 MM

	s	x	2006	2007	2008
s				-	-
x					
c					
c					
v					
v					
s					
s					
c					

Key assumptions:

- Same profile and peak share assumptions as U.S. forecast
- Price (ASP) = \$0.30 per day, or \$27 per 30 day Rx (comparable to COX-2 pricing)
- Average AI launch assumption is Q1 2005 to allow for additional regulatory filings (COFCG and national filings in PAA and LA) and/or pricing negotiations (most markets in Europe) required in AI markets

Forecast Update Plan:

Forecast will be updated pending analysis of Phase IIb clinical trial results (March or April 2003) or before if the clinical trial plan changes from current assumptions.

C.4.3 Global Sales Forecast

The global sales forecast is shown in Table C.4.3, below.

Table C.4.3 Global Forecast					
	2008	2009	2010	2011	
U.S. Sales (\$MM)	\$53.1	\$140.1	\$246.4	\$342.6	\$446.9
Ex-U.S. Sales (\$MM)	\$89	\$139	\$231	\$312	\$392
Total Sales (\$MM)	\$142	\$279	\$477	\$654	\$838
Total Company Margin (\$MM)	\$26.9	\$45	\$75.5	\$112.2	\$159.8

10 year pre-tax NPV @ 12.5% = \$
10 year post-tax NPV @ 12.5% = \$
MM

Deleted: Table C.4.2. Ex-U.S. Forecast (Date of Forecast: 6/98)

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Deleted: 2005

Deleted: Market Rxn (MM) - % chg

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Deleted: Abbott Share (%)

Deleted: Abbott Rxn (MM)

Deleted: Pricer/R_t (%)

Deleted: Abbott Sales (\$MM)

Deleted: R&D (\$MM)

Deleted: SG&A (\$MM)

Deleted: SMM (%)

Deleted: Div. Margin (\$MM)

Deleted: 10 year pre-tax NPV @ 12.5% = \$428

Deleted: 10 year post-tax NPV @ 12.5% = \$253

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- Deleted: First in class GABA_A
- Indicated for treatment of moderate to moderate-severe pain
- Effective in neuropathic pain
- Good tolerability and safety profile
- No-metabolite effects (impossible as then wouldn't work!) No addictive potential
- Launched in all AI regions, including Japan, simultaneously (2003)

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C.5 Facilitating Launch and Market Penetration

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ABT-594 will hopefully be the first neuronal nicotinic receptor drug to market presenting both opportunity and hurdles. Significant pre-launch activities aimed at increasing understanding of NNR drugs and countering any concerns regarding their association to nicotine will be needed. A comprehensive communication plan will be needed and is discussed in detail below. Research to ensure in-depth understanding of the changing analgesic market and ABT-594's optimal position within that market will need to be conducted periodically up to launch. Opinion leaders in NNR science, general pain management, osteo and rheumatoid arthritis, and diabetic and other neuropathies will be important in the peri-launch period as spokespeople and educators and need to be kept up to date on activities throughout ABT-594's development. These and additional activities to facilitate launch are outlined in Table C.5.1 below.

C.5.1 Activities to Facilitate Launch and Market Penetration	
ACTIVITY	PURPOSE
Pain Specialist Advisory meetings	Permits up to date knowledge of market science and pain treatment trends while building base of supportive, receptive opinion leaders with in-depth knowledge of ABT-594 (and entire neuronal nicotinic receptor program)
Medical education	Primes market with information regarding advances in pain management and introduces neuronal nicotinic receptor class to speed market familiarity and uptake
Information dissemination to publishers	Allows for discussion of class to be included in texts, professional newsletters, pharmacy alerts, etc. to build awareness and understanding of technology (NNR) pre-launch
Managed Care Director Advisories/Roundtables	Allows Abbott to gain understanding of reimbursement environment for pain products, key data that MCOs will need for formulary decisions to potentially include in Phase III clinical trial design
Publication of NNR and ABT 594 specific data at key meetings and in professional journals	Prime market with information regarding advances in pain management and introduce neuronal nicotinic receptor class to speed market familiarity and uptake
Public Relations Activities (media releases, etc.)	Increase general public's comfort level of nicotinic nomenclature particularly regarding the safety and lack of addictive potential for these drugs; may also generate excitement and pull-through demand
Market Research	Determine key drivers of pain prescribing, critical data points, entry niches, and compelling key messages

C.5.2 Communication Strategy~~Deleted: [Andrea/Laura to review]~~

A comprehensive communication strategy for ABT-594 as a stand alone product and as the first product of the neuronal nicotinic receptor (NNR) class is in development. Due to the importance of the entire NNR program, a specialized communications strategy vendor (Ingenix) will be working with the internal ABT-594 team to craft the plan. The overall NNR program strategy will be focused on maximizing the market potential for ABT-594 and other compounds by:

- positioning these agents as novel, effective and safe
- generating awareness and educating prescribers and consumers about the NNR class and ABT-594 specifically
- establishing Abbott as the market leader in NNR science

Key to success of this strategy will be the cohesive, coordinated, and aligned efforts of R&D, commercial and public affairs. NUDR Discovery, the Analgesia Venture, NPD, AI NPP, and Public Affairs will work together with the vendor to lay out comprehensive Scientific, Marketing, and Public Relations plans that will outline communication timing, content, audience, and venue for all ABT-594 data. The primary goals of the communication strategy will be:

- position Abbott as the leader in NNR drug development
- augment internal development efforts
- build a base of supportive opinion leaders
- allay consumer concerns regarding the association of these compounds with nicotine
- build a framework for NNR product positioning
- generate market awareness for upcoming product launches

A complete communication strategy publication will be prepared during the third quarter of 2000.

H.5 Patent Issues [Andrea/Jim S. to review] getting copy of patent to consider if we need to explore expanding its scope.

A notice of allowance has been obtained from the United States Patent and Trademark Office on an application providing generic coverage for ABT-594 and a large class of structurally related analogs. The original filing date for this application dates back to October 9, 1992, and since this predates a 1996 change in patent law, we are afforded a choice of 20 years from date of filing or 17 years from date of issue, of which 17 years from issue provides the longer patent life. The anticipated expiration of patent coverage for composition of matter for ABT-594 will be June, 2016. An additional application (6013.US.01), which includes species claims to ABT-594 as well as use claims for the treatment of pain, was filed in December, 1996 and is pending. If this patent is allowed, it will provide 20 years from date of filing, which will extend the patent life of ABT-594 to December, 2016.

24

The original application providing generic composition of matter coverage was filed broadly ex. U.S. (WO94/08992) and this application published on April 28, 1994. A second foreign filing (WO96/40682) published on December 19, 1996. These cases are all still pending.

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Addenda

1.1 Highlights re: ABT-594

1.2 Historical Changes to ABT-594 Target Product Profile

- At PPCC, indications considered for ABT-594 were acute vs. chronic pain, with an acute pain claim being considered to have a shorter development course (if long term toxicology studies were not required).
- The FDA (3/98) related their concern that an oral dosage form may be used for chronic therapy even if labeled for acute. Long term toxicology would be required, therefore, even for acute claims.
- Decision analysis review of the program (3/98 - 7/98) arrived at several conclusions:
 - A general pain indication associated with a longer development cycle had greater value than an acute indication associated with a shorter development cycle.
 - Carcinogenicity studies should be initiated prior to first Phase II results.
 - Follow-on compounds (in the same cholinergic channel modulator class and in different pharmacologic classes) should be developed.
- Data from the first Phase II study (single dose molar extraction) indicated that ABT-594's onset of action is 1.5 - 2 hours post dose. Because a general pain indication requires efficacy in acute pain states (with more rapid onset of action), ABT-594 was considered unlikely to achieve a general indication. The current clinical plan targets disease-specific chronic pain indications.

The global target indications for ABT-594 are for the treatment of pain associated with diabetic neuropathy and for the treatment of pain with osteoarthritis.

Landsberg Deposition Exhibit 10

P's Exhibit SM



Bruce
McCarthy /LAKE/PPRD/ABB
OTT
10/03/2000 08:04 AM

To: Andrea Landsberg/LAKE/PPD/ABBOTT@ABBOTT
Robert J Weiland/LAKE/PPD/ABBOTT@ABBOTT,
Rosemarie K Waleska/LAKE/PPD/ABBOTT@ABBOTT,
Christopher J Silber/LAKE/PPRD/ABBOTT@ABBOTT,
cc: George W Carter/LAKE/PPRD/ABBOTT@ABBOTT, Mike
Williams/LAKE/PPRD/ABBOTT@ABBOTT, James
Sullivan/LAKE/PPRD/ABBOTT@ABBOTT, Larry L
Lin/LAKE/PPD/ABBOTT@ABBOTT
bcc
Subject: Re: ABT 594/963 Purdue meeting

No problem from my perspective. As far as co-development, I think there are some exciting possibilities with Purdue (financials aside). My expectation is that Purdue should be very sophisticated in terms of product development (commercial and clinical) for the chronic pain market. In addition, Lynn Kramer (now VP of Neuroscience there, formerly of Novartis) has extensive neuroscience/pain drug development experience and Curtis Wright (heads up neuroscience/pain development there, formerly of the FDA) has defined the regulatory requirements for pain drugs. Curtis may be a little bit of an unknown variable, though. Although he is the Paul Leber for pain, he has jumped around a bit since leaving the FDA. There may not be a guarantee that he'll stay at Purdue for long. In any event, if we meet with Purdue, I think we should very carefully test their knowledge from a commercial and development perspective

Andrea Landsberg



Andrea Landsberg
10/03/2000 07:32 AM

To: Robert J Weiland/LAKE/PPD/ABBOTT@ABBOTT
cc: Rosemarie K Waleska/LAKE/PPD/ABBOTT@ABBOTT, Christopher J
Silber/LAKE/PPRD/ABBOTT@ABBOTT, Bruce McCarthy/LAKE/PPRD/ABBOTT@ABBOTT, George W
Carter/LAKE/PPRD/ABBOTT@ABBOTT, Mike Williams/LAKE/PPRD/ABBOTT@ABBOTT, James
Sullivan/LAKE/PPRD/ABBOTT@ABBOTT, Larry L Lin/LAKE/PPD/ABBOTT@ABBOTT
Subject: ABT 594/963 Purdue meeting

Bob,
As you, Rose and I had discussed, if we move forward to set up a presentation of information to Purdue, the following people could probably do the presenting on key topics

Preclinical ABT 594:	Jim Sullivan
Clinical ABT 594:	Bruce McCarthy
Preclinical and Clinical Plan ABT 963:	George Carter
Market Opportunity/Business Rationale:	Andrea Landsberg

If anyone has objections or would like to suggest alternate individuals, please feel free to do so

One final comment that I neglected to bring up yesterday: George and I have had a number of conversations regarding the meaning of 'co-development' and the potential impact on development costs and timelines. I think this needs to be the topic of a separate discussion so that we can clearly define 'co-development' on our terms prior to any negotiations with a partner. Of course, Chris and the analgesia venture's input would be key in this discussion

Andrea

Andrea DEP. EX. NO. 10
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P's Exhibit DG



Andrea
Landsberg /LAKE/PPD/ABBO
TT
10/27/2000 12:57 PM

To Christopher J Silber/LAKE/PPRD/ABBOTT@ABBOTT,
rosemarie waleska
cc
bcc
Subject 594 Leiden presentation

Here is a first draft of the 594 slides; you will see that there are a few pieces of information that I do not have available with me on the road but will fill in when back in the office. Please provide any comments/suggestions that you have.

Thanks,
Andrea

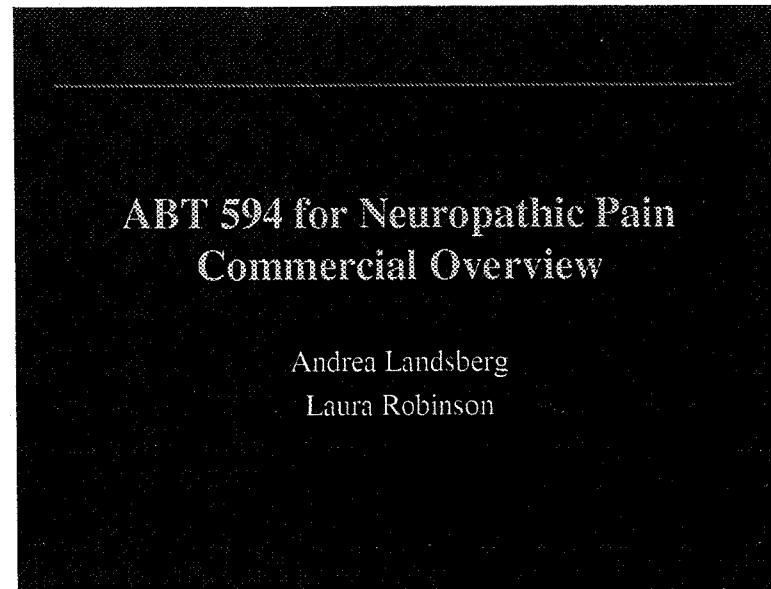
I am beginning work on the ABS/NPS slides now!

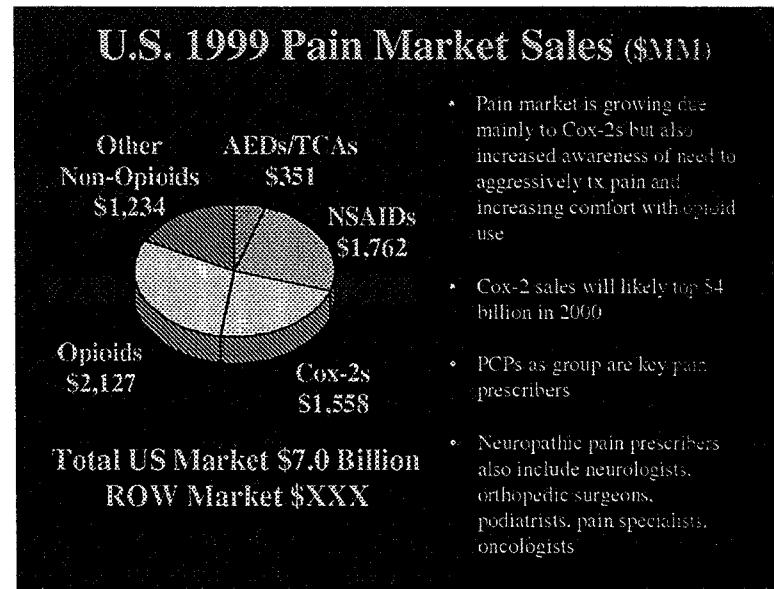


leiden presentation - Nov

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FOR ID., AS OF 2-16-07 BC

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Pain Markets Considered for ABT 594

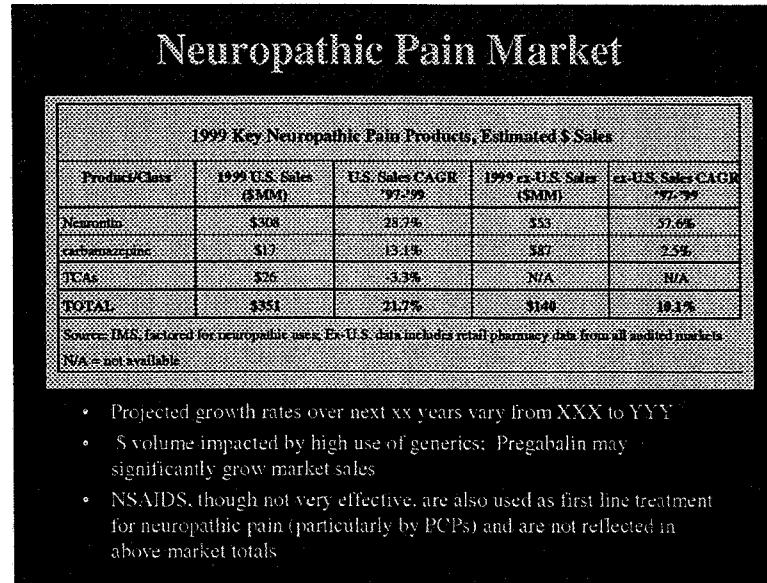
- Acute and chronic pain
- Chronic pain
 - nociceptive and neuropathic
- OA/RA
- Neuropathic pain
 - diabetic polyneuropathy pain
- Moderate to moderately severe pain

ABT 594: Current vs DDC Profile

DDC Profile (12/97)	Current Profile (9/00)
• Indicated for the treatment of pain (general pain claim)	• Indicated for the treatment of neuropathic pain. Efficacy in OA demonstrated in non-indication trial
• Improved safety profile compared to opioids including: - less GI motility impairment - less respiratory depression - low tolerance potential - no dependence/withdrawal	• In contrast to opioids, no constipation or respiratory depression liability • In DPN, potentially high (>30%) discontinuation rates due to vomiting
• No titration	• Titration to minimize SEs
• Onset of action in less than 30 minutes	• Onset of action at 1.5 to 2 hours

Indication and Spillover Potential

- Market research conducted x/99?
- Make table with share% in various markets depending upon indication
- clarify product profile in study vs current knowledge

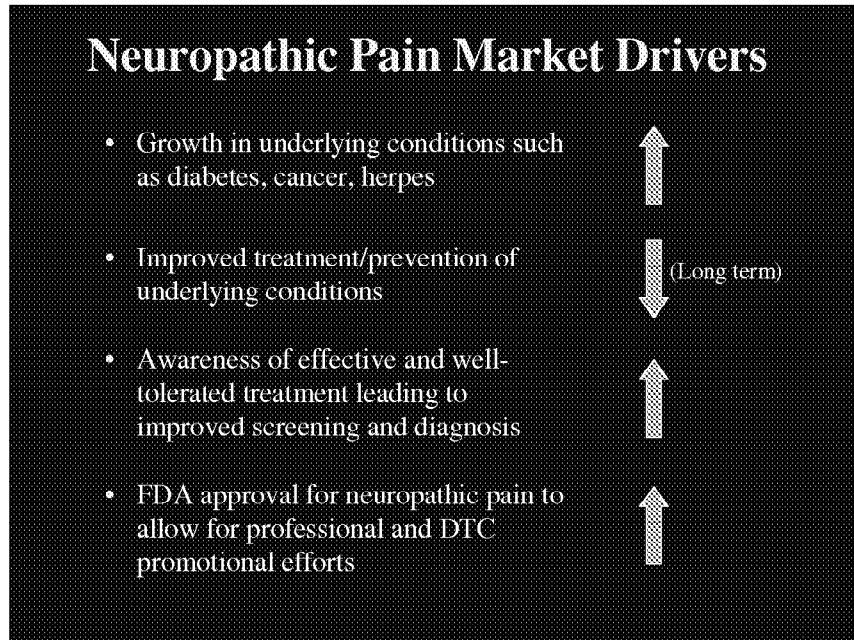


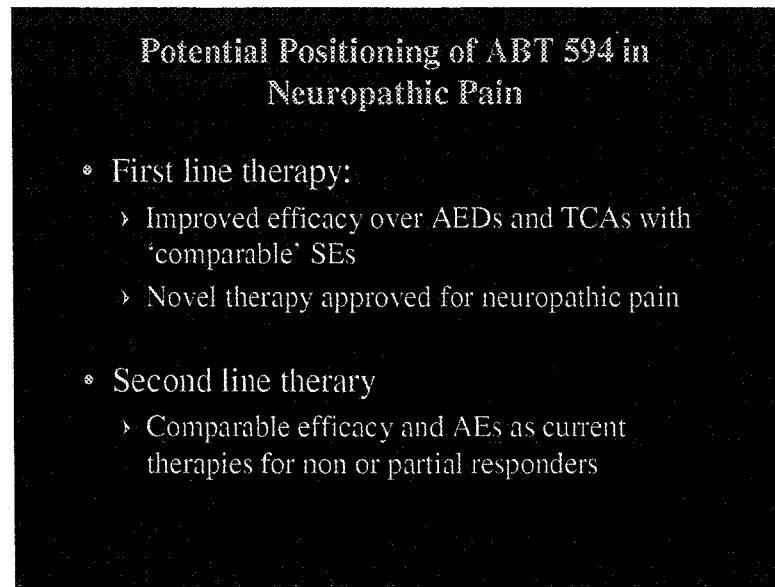
Neuropathic Pain Competition

Product	Price	Cost
NSAIDS/COX-2s	Often used first line by PCPs COX-2s increasing comfort with chronic use Generally inexpensive except for COX-2s	Generally low efficacy in neuropathic pain
TCA's (amitriptyline, nortriptyline, etc.)	Generally effective Inexpensive	Off-label use Side effects (dry eye, weight gain, anticholinergic syndrome) Risk of overdose Titration required
Neurontin (gabapentin)	Good efficacy, considered first line treatment Some well controlled positive trials	Off label use (2/3 patients may not experience pain relief) Titration required; high doses required (high pill burden) TID dosing Expensive, though will be off-patent by time of ABT 249 launch Somnolence, dizziness, cognitive side effects Not indicated for pain (except in UK)
Pregabalin	Initial data in neuropathic pain very promising Lowers doses than with Neurontin Likely to pursue indication in pain	TID dosing (less titration?) Off label for Neurontin; low D/C rates Initial Two trials in chronic low back pain failed to show significant efficacy

Unmet Needs in Neuropathic Pain

- More complete efficacy than that provided by Neurontin
 - including increase in responder rate
- Efficacy matching Neurontin, with reduced side effects
- Treatments with reduced or no titration
- Improved dosing schedules, ideally QD
- Formulation options for single compound
 - patch, parenteral, solution, sprinkle, melt

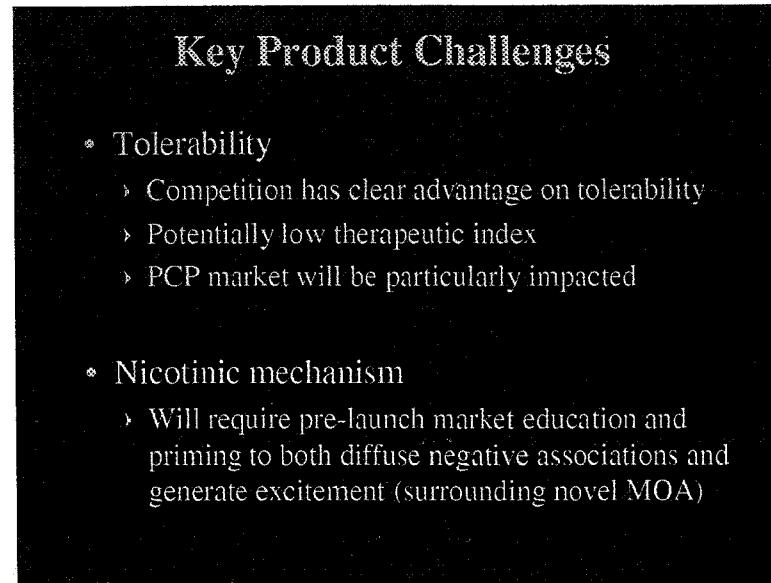


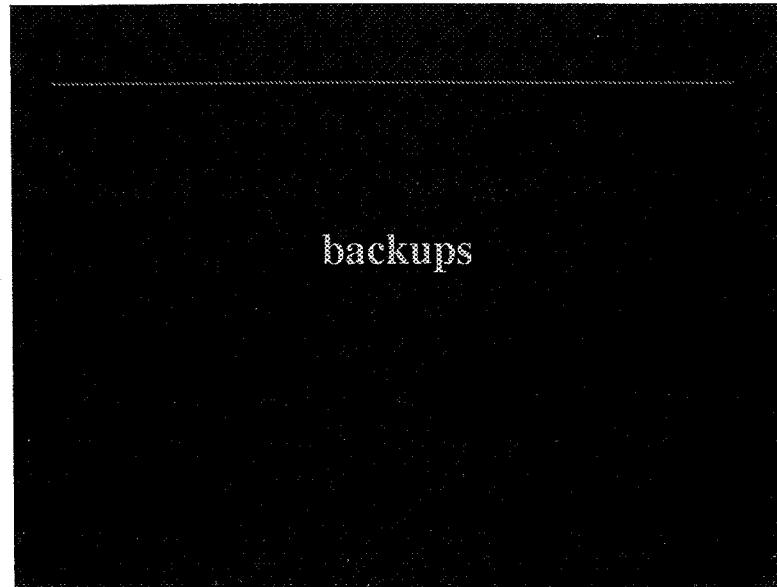


ABT 594 Forecast			
	U.S.	ROW	Total
Peak Sales	\$447 MM	\$xxx MM	\$xxx MM
Peak Share			
Neuropathic	20%	20%	NA
Persistent Nociceptive	10%	10%	
NPV @ 12.5% (in \$MM)	\$422 MM	\$215 MM	\$637 MM

ABT 594 Forecast Assumptions

	US	ROW
Indication	Neuropathic pain (published study of efficacy in OA in 2006)	
Key dates	NDA filed 9/03 Approval 9/04	
Order of entry	First analgesic to market for pain	
Safety	No addiction liability No major safety concerns	
AWP/Day	\$3.75	
Dosing	75-150mg BID; 3-5 day titration	
Efficacy	Greater than Meperidine in neuropathic and COX-2s in nociceptive	
Tolerability	CNS SEs improved over Meperidine; GI SEs improved over tramadol	
COGS	\$216K/kg (small volume)	

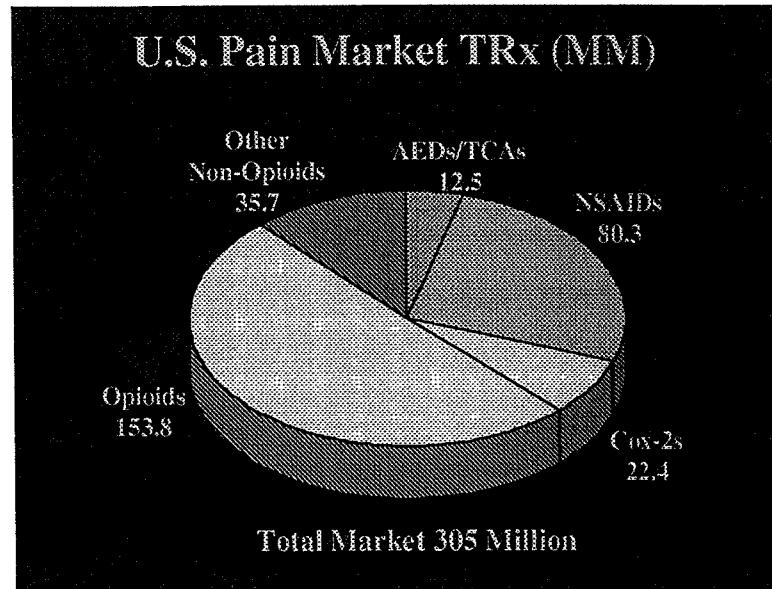




Complexity of Segmenting the Pain Market

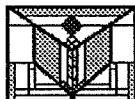
- Pain Market can be segmented in a variety of ways
 - Duration
 - Peracute, Acute, Chronic
 - Severity
 - Mild, Moderate, Severe
 - Pathophysiology
 - Neuropathic, Nociceptive, Mixed
 - Etiology
 - Cancer, Injury, Infection, Metabolic (DPN), Immunologic (OA/RA), etc.
- Each classification is relevant for almost every pain patient

	TRx CAGR 97-99	Sales CAGR 97-99
AEDs	26.3%	28.7%
TCAs	8.2%	-3.3%
NSAIDs	-1.3%	-3.9%
Cox-2s	NA	NA
Opioids	2.5%	8.2%
Other Non-Opioids	-1.0%	-3.8%



Landsberg Deposition Exhibit 18

P's Exhibit DS



Michael K
Bjarnesen/LAKE/PPRD/ABB
OTT
11/29/2000 02:11 PM

To Andrea Landsberg/LAKE/PPD/ABBOTT@ABBOTT
cc Christopher J Silber/LAKE/PPRD/ABBOTT@ABBOTT,
Bruce McCarthy/LAKE/PPRD/ABBOTT@ABBOTT
bcc
Subject Re: ABT 594 forecast scenarios for BD partnering

Andrea,

Here is what Chris and I worked up for the Label/ Development Cost scenarios. We have included different scenarios, so after you have a chance to review, let's get on the phone and reconcile, OK?

Mike B



ABT-594 Partner.ppt
Andrea Landsberg

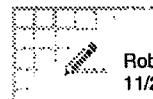
Andrea Landsberg

11/29/2000 10:40 AM

To: Robert J Weiland/LAKE/PPD/ABBOTT@ABBOTT
cc: Larry L Lin/LAKE/PPD/ABBOTT@ABBOTT, Christopher J Silber/LAKE/PPRD/ABBOTT@ABBOTT,
Michael K Bjarnesen/LAKE/PPRD/ABBOTT@ABBOTT, Bruce
McCarthy/LAKE/PPRD/ABBOTT@ABBOTT, Rosemarie K Waleska/LAKE/PPD/ABBOTT@ABBOTT
Subject: Re: ABT 594 forecast scenarios for BD partnering

Need to titrate this drug to (any) effective level, therefore that cuts us out of any 'acute' or chronic but intermittent type of use; Oxycontin may need to be titrated to max efficacy and dose may need to be increased if tolerance develops but it still can be given at a dose that is likely to provide some pain relief right off the bat. This has been the thinking since the phase IIa results were in

Robert J Weiland



Robert J Weiland
11/29/2000 10:13 AM

To: Andrea Landsberg/LAKE/PPD/ABBOTT@ABBOTT
cc: Larry L Lin/LAKE/PPD/ABBOTT@ABBOTT, Christopher J Silber/LAKE/PPRD/ABBOTT@ABBOTT,
Michael K Bjarnesen/LAKE/PPRD/ABBOTT@ABBOTT, Bruce
McCarthy/LAKE/PPRD/ABBOTT@ABBOTT, Rosemarie K Waleska/LAKE/PPD/ABBOTT@ABBOTT
Subject: Re: ABT 594 forecast scenarios for BD partnering

Andrea:

This looks like a decent starting point. Oxycontin will do over \$1 billion by itself. I am wondering if our upsides don't take us well over the \$1 billion mark?

BW

Andrea Landsberg

Andrea Landsberg

11/29/2000 07:17 AM

Sandsberg DEP. EX. NO. 18
FOR ID., AS OF 2-10-07 BC

CONFIDENTIAL
ABBT0119091

To: Larry L Lin/LAKE/PPD/ABBOTT@ABBOTT, Christopher J Silber/LAKE/PPRD/ABBOTT@ABBOTT,
Michael K Biarnesen/LAKE/PPRD/ABBOTT@ABBOTT, Bruce
McCarthy/LAKE/PPRD/ABBOTT@ABBOTT
cc: Rosemarie K Waleska/LAKE/PPD/ABBOTT@ABBOTT, Robert J Weiland/LAKE/PPD/ABBOTT@ABBOTT

Subject: ABT 594 forecast scenarios for BD partnering.

I have made some initial slides and forecast estimations that take the 594 forecast up in steps based on potential additional studies. I have done this 2 ways: one starting from the development plan forecast (Mike: the revised one that has the updated NP market size plus the launch delay, not the one in the 'draft' development plan) and one starting one step back from there without any study in a chronic nociceptive pain state. Please let me know ASAP if these steps will be acceptable and whether rough costs for these hypothetical programs can be determined.

Larry, please let me know if these numbers look acceptable-- some of them may already be optimistic -- BD's call as to whether you want to inflate them for 'best case' scenario.

Andrea



BD partnering slide on insides to be

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ABBT0119092

ABT 594 Forecast Potential

Scenario	Peak Sales (\$MM)
Indication in DPN w/ nociceptive publication	\$507
Above plus additional neuropathic pain states pub	\$629
Above plus opioid sparing publication	\$746
Above plus OA or other nociceptive indication	\$1009

DNP = Diabetic neuropathic pain

Scenario	Peak Sales (\$MM)
Development Plan Base	
Indication in DPN w/ nociceptive publication 20% share NP, 10% CPP	\$507 +122
Above plus additional neuropathic pain states pub. additional 10% share of NP (total share of 30%)	= \$629 +117
Above plus opioid sparing publication 10% share of 75% of 'strong opioid market' (generics) (morphine, synthetic opioid, oxycodone)	= \$746 +263
Above plus OA or other nociceptive indication additional 10% share in CPP (total share of 20%) -- optimistic.	= \$1009

NP = neuropathic pain, CPP = chronic persistent (nociceptive) pain

ABT 594 Forecast Potential

Scenario	Peak Sales (\$MM)
Indication in DPN	\$235
Above plus additional neuropathic pain state pub.	\$365
Above plus nociceptive publication	\$628
Above plus opioid sparing publication	\$745
Above plus OA indication	\$1008

ABT 594 Forecast Potential

Scenario	Peak Sales (\$MM)
Indication in DPN	\$235
20% share NP	+122
Above plus additional neuropathic pain state pub.	=\$365
additional 10% share of NP (total share of 30%)	+263
Above plus nociceptive publication	=\$628
10% share of CPP	+117
Above plus opioid sparing publication	=\$745
10% share of 75% of 'strong opioid market' (morphine, synthetic opioids, oxycontin) (generous)	+263
Above plus OA indication	=\$1008
additional 10% share in CPP (total share of 20%) -- optimistic	

Landsberg Deposition Exhibit 19

P's Exhibit EB



Jennifer
Dart/LAKE/PPRD/ABBOTT
12/21/2000 11:35 AM

Christopher J Silber/LAKE/PPRD/ABBOTT@ABBOTT,
Michael K Biarneser/LAKE/PPRD/ABBOTT@ABBOTT,
Bruce McCarthy/LAKE/PPRD/ABBOTT@ABBOTT, Andrea
Landsberg/LAKE/PPD/ABBOTT@ABBOTT, Laura
To: Robinson/LAKE/AI/ABBOTT@ABBOTT, Barbara T
Massa/LAKE/PPRD/ABBOTT@ABBOTT, Steve C
Kuemmerle/LAKE/PPRD/ABBOTT@ABBOTT, George W
Carter/LAKE/PPRD/ABBOTT@ABBOTT, Chris G
Turner/LAKE/PPRD/ABBOTT@ABBOTT
cc: Richard J Marasco/LAKE/PPD/ABBOTT@ABBOTT
bcc: Analgesia Internal Review Notes

Thanks to everyone for your participation in the Analgesia Internal Review.

Andrea, Laura or Chris: will one of you please set up some time with Rock to review the project assumptions and forecasts.

As a reminder, final forecasts are due to Chris Turner on Monday, January 15th, although we would greatly appreciate receiving them before then if possible.

Following is the list of follow up items from the meeting:

ABT-594

- Andrea will reduce forecast to reflect vomiting AE
- Osteo project will change name to Chronic Persistant Pain Publication (CPPP)
- Steve Kuemmerle will research whether the CPPP probability of success should be reduced to 16% since this project is contingent upon Neuro Pain project success

ABT-089

- Laura & Andrea to review forecast assumptions
- Need to check COGS estimate
- Probability of success revised to 18%

Hydrocodone -

- Forecasts will be submitted prior to January 1. We can review these forecasts at the ABS/NPS review scheduled for January 10th.
- Rapid Dissolve probability of success reduced to 35% due to RP Scherer DEA import issues

General

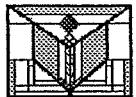
- Patent expiration dates need to be confirmed for all compounds
- R&D spending ends at launch

Landsberg 19
DEP EX 2-16-07 BC
FOR ID., AS OF 2-16-07 BC

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ABBTO108041

Landsberg Deposition Exhibit 26

P's Exhibit EJ



Michael K
Biarnesen/LAKE/PPRD/ABB
OTT
02/01/2001 01:11 PM

To: Christopher J Silber/LAKE/PPRD/ABBOTT@ABBOTT,
Bruce McCarthy/LAKE/PPRD/ABBOTT@ABBOTT
cc:
bcc:
Subject: Re: financial slides for Leiden meeting 2/2

FYI

----- Forwarded by Michael K Biarnesen/LAKE/PPRD/ABBOTT on 02/01/2001 01:11 PM

Andrea Landsberg

02/01/2001 10:34 AM

To: Thomas E Woidat/LAKE/PPRD/ABBOTT@ABBOTT
cc: Michael K Biarnesen/LAKE/PPRD/ABBOTT@ABBOTT
Subject: Re: financial slides for Leiden meeting 2/2

Tom,

As per your request to Mike -- this is not all of the slides that will be shown but just those with financial info -- please let me know if there is anything else you require.

Andrea



ART-089 Leiden Presentation Commercial fin ART-594 Leiden Presentation Commercial fin



ART-089 Port Qua final 1. ART-594 neuropathic pain · ART-594 publication study ·

Landberg EX. NO. 26
02-16-07
FOR ID., AS OF

ABT 594 Global Forecast Ranges			
	(\$MM)		
	Peak Sales		
	Low	Base	High
US	\$92	\$339	\$509
Ex-US	\$130	\$363	\$712

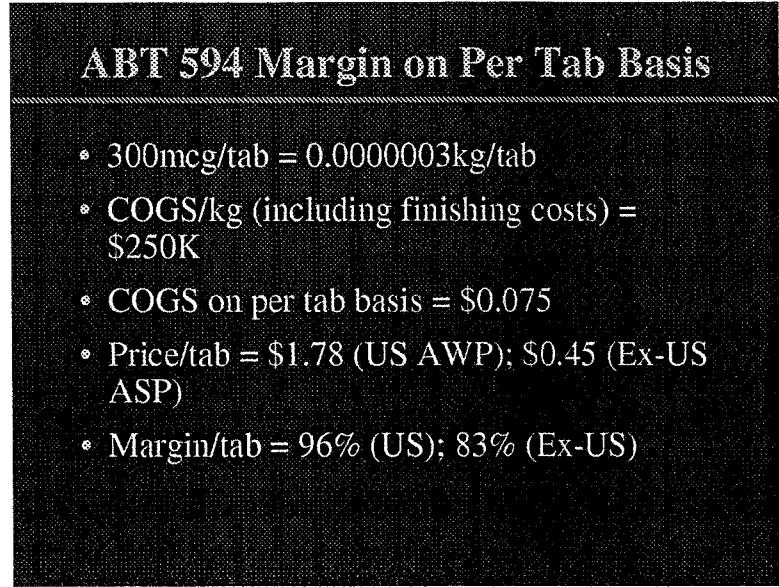
*NP shares: 5%, 20% or 30%
•CPP shares: 3%, 5%, 7%

ABT 594 Global Forecast Ranges						
	Peak Sales			NPV		
	Low	Base	High	Low	Base	High
US	\$92	\$339	\$509	\$2	\$313	\$522
Ex-US	\$130	\$363	\$712	\$55	\$356	\$857

ABT 594 Pricing

- US launch price \$3.57/day (AWP)
 - Comparable to Neurontin/Cox 2 daily AWP (in 2004)
 - Should be supportable - one of few drugs indicated for NP and a novel mechanism
 - Forecasting assumes reasonable discounting to ensure MC coverage and penetration
- Ex-US launch price \$0.90/day (ASP)
 - Comparable to premium priced pain drugs (COX-2)
 - Unlikely to match Neurontin price, as ABT-594 will likely be reference-priced vs. analgesics, not AEDs

Used in base case forecast, 1/01



ABT 594 Promo and Sales Force Spend														
	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Promo spending (\$MM)	2	30	50	35	50	39	25	25	25	20	20	20	15	6
Direct to Customer spending (\$MM)	0	2	1	3	1	0	0	0	0	0	0	0	0	0
FR spending (\$MM)	3	3	2	2	1	0.5	0.5	0.3	0.3	0.2	0.2	0	0	0
Total Promo excluding samples	5	35	56	38	52	36.5	25.5	25.3	25.3	20.2	20.2	20	15	6
TOTAL PROMO EXPENSE	5.0	37.8	56.4	31.6	53.9	32.7	27.7	27.9	26.7	21.6	21.2	22.6	21.2	12.2
Sales (\$MM)	N/A	27.4	98.4	170.5	231	291.7	330.3	316.2	305.8	297.9	292.1	285.1	274.8	260.1
% of Sales		1.8%	61%	24%	15%	11%	8%	8%	9%	7%	7%	8%	8%	6%
	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Total Sales Force Expense (\$MM)		13.2	35.6	24.6	21.7	25.5	26.5	23.0	20.6	17.5	18.5	13.8	19.1	

ABT 594 Base Case Forecast		
	U.S.	Ex-US
Peak Sales	\$339 MM	\$363 MM
Salesforce/Promo	\$54MM	\$34MM
Peak Share		
Neuropathic	20%	20%
Chronic Persistent	5%	5%
NPV @ 12.5% (after tax)	\$313 MM	\$356 MM

Landsberg Deposition Exhibit 28

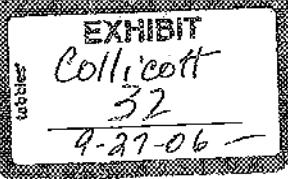
P's Exhibit EL

Part I

Project Review

ABT-0002314 ABT-0002314

February 2, 2001



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ABBT 0002314
J. Landberg
DEP EX NO 26
FOR ID... AS OF 2-16-07
2-16-07

Project Review

ABT-089

REDACTED

ABT-594

— Overview, Upcoming milestone: June 2001
— Follow-on strategy

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ABBT 0002316

**NEUROTOMAL NICOTINIC RECEPTOR
(NNR) Program**

- Scientific leadership position for Abbott
- An emerging diversity of receptors
- Multiple potential therapeutic targets

ABT-089

REDACTED

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ABBT 0002317

ABBT-089

REDACTED

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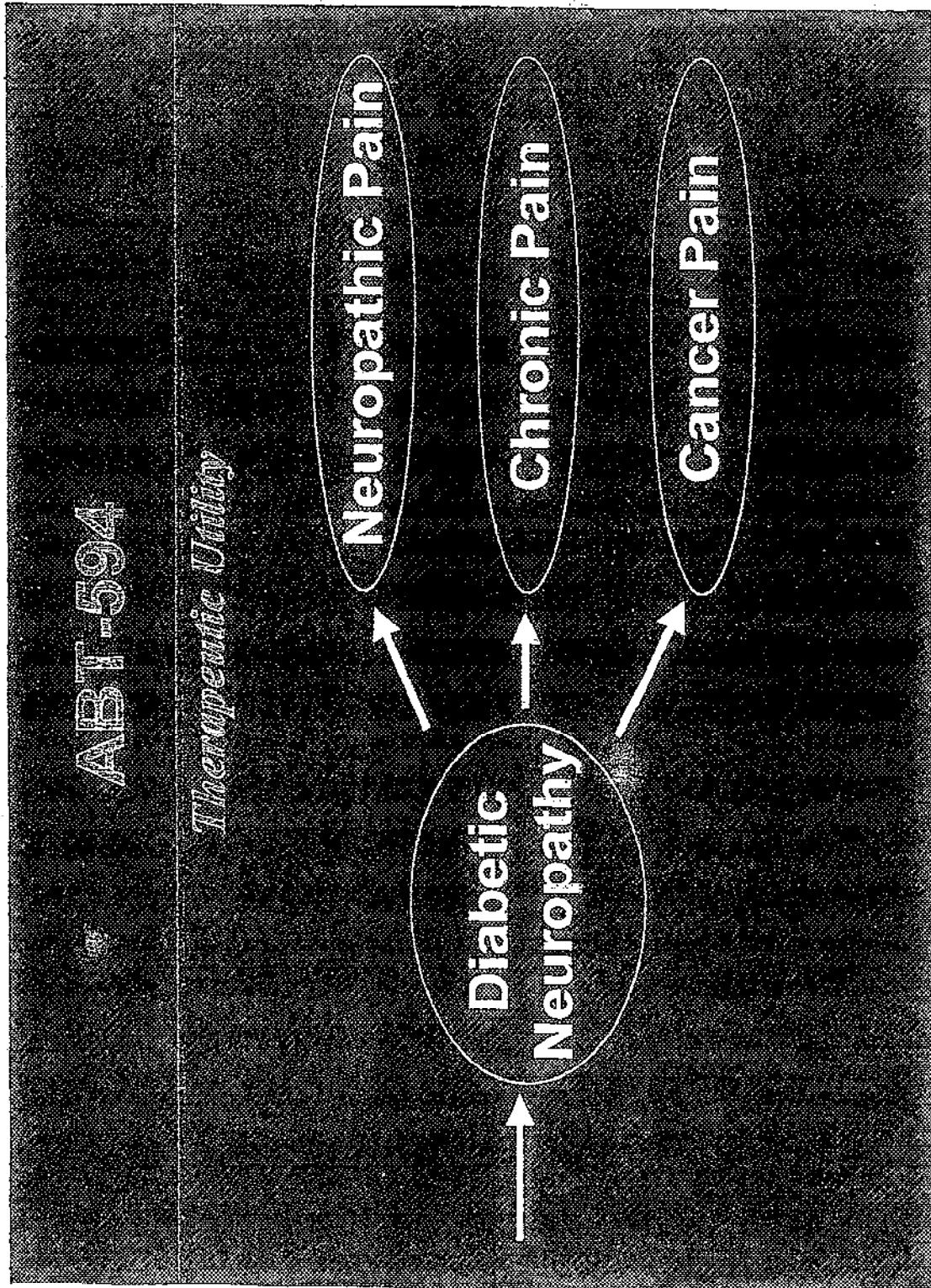
ABBT 0002318

ABT-594

Overview

First-in-class

- o Analgesic potential demonstrated at 75 mcg BID
- o Dizziness (7%), nausea (15%), vomiting (5%) observed at 75 mcg BID
- o Full efficacy not determined
- o MTD is 300 mcg BID
- o Phase IIb in painful diabetic neuropathy, using doses up to 300 mcg BID ongoing
- o Global sales: \$700 MM



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ABT 0002320

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ABBT 0002321

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Landsberg Deposition Exhibit 28

P's Exhibit EL Part II

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ABBT 0002363

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P's Exhibit EL

Part 3

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ABBT 0002358

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P's Exhibit EL

Part 4

ABT 504 Project Review

February 2, 2001

Introduction

Chris Silber

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ABT 0002359

AETT-594 Project Review

Agenda

Introduction

Chris Silber

Pharmacological Profile

Jim Sullivan

Clinical Overview

Bruce McCarthy

Commercial Assessment

Andrea Landsberg

Go/No Go Process

Bruce McCarthy

Follow-On Strategy

Mike Meyer

Landsberg Deposition Exhibit 28

P's Exhibit EL Part 5

ABT-594

Overview

- First-in-class
- Analgesic potential demonstrated at 75 mcg BID
- Dizziness (7%), nausea (15%), vomiting (5%) observed at 75 mcg BID
- Full efficacy not determined
- MTD is 300 mcg BID
- Phase IIb in painful diabetic neuropathy, using doses up to 300 mcg BID ongoing
- Global sales: \$700 MM

Pain Prevalence

- 22% primary care patients worldwide have persistent pain
- Neuropathic pain
 - 20% of diabetics
 - 40% of HIV infected
 - 36% of cancer patients

Pain Therapeutics Market

\$12 billion in sales of key classes
(NSAIDs, COX-2s, Opioids, non-opioids)

\$700 million in sales of key
neuropathic pain compounds
— Use largely off-label
— Low cost generics

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ABBT 0002383

Neuropathic Pain

Treatment

Some efficacy
(at best 40% vs. 20% placebo)

◦ Tricyclic antidepressants

– Amitriptyline, desipramine, etc.

◦ Anti-epileptic drugs

– Carbamazepine

– Gabapentin (Pregabalin)

– Topiramate, others

◦ Sodium channel blockers

– Lidocaine

◦ Opioids

– Tramadol

No efficacy

◦ SSRIs

◦ NSAIDs/COX-2

**Broad-Spectrum, Non-Opioid Analgesic Activity
by Selective Modulation of Neuronal Nicotinic
Acetylcholine Receptors**

A. W. Bannon, M. W. Decker, M. W. Holladay, P. Curzon,
D. Donnelly-Roberts, P. S. Puttfarcken, R. S. Bitner, A. Diaz,
A. H. Dickenson, R. D. Porsolt, M. Williams, S. P. Americ

SCIENCE, VOL. 279 • 2 JANUARY 1998

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ABBT 0002366

DeviQOITment Strategy

Acute

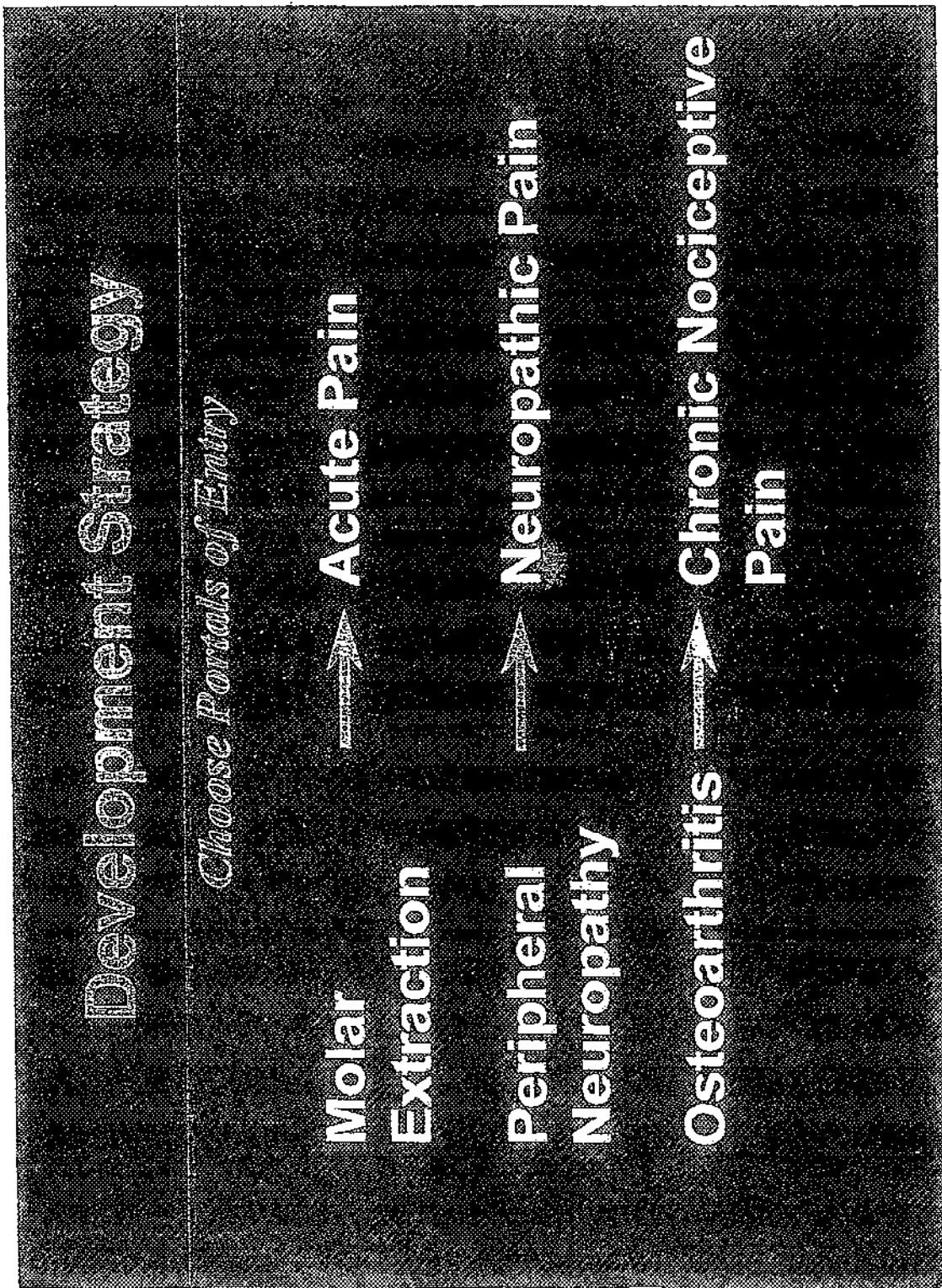
Post-dental surgery
Strains and strains
Acute back pain
Trauma
Post-general surgery
Post-orthopedic
surgery
Dysmenorrhea
Renal colic
Biliary colic
Pancreatitis
Infections

Neuropathic

Diabetic polyneuropathy
Idiopathic polyneuropathy
Alcoholic polyneuropathy
Drug-induced polyneuropathy
HIV predominant sensory
neuropathy
Back pain
Cancer pain
Trigeminal neuralgia
Post-herpetic neuralgia
Thalamic pain syndromes
Spinal cord injury
Multiple sclerosis
Complex regional pain
Syndromes (1, 1)
Atypical facial pain
Phantom limb pain

Chronic Nociceptive

Osteoarthritis
Chronic back pain
Rheumatoid arthritis
Cancer pain
Fibromyalgia
Sickle cell disease
TMJ disorder
Bursitis
Tendinitis
Chronic visceral pain



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ABBT 0002367

ABT-594

Current Label Targets

ABT-594 is indicated for the treatment of
diabetic neuropathic pain.

Upside Claim

- Neuropathic Pain
- Post herpetic neuralgia
- OA Pain
- Chronic Pain
- Cancer Pain

General Pain Claim

- Not viable due to
1.5 hour onset

Landsberg Deposition Exhibit 28

P's Exhibit EL

Part 6

ABT-594

Go/No Go Process

Decision analysis (DSG) will be used as a tool to determine milestone criteria

- Efficacy and safety
- Toleration effects
- Dose selection
- Indications
- Market research

ABT-594

Phase III Clinical Plan

	U.S.	Europe	Japan	
Diabetic neuropathy	2 (n=1200)	2 (n=1200)	1 (n=300)	
Long-term safety	1 (n=500)	1 (n=500)	-	
Gabapentin comparator	-	-	1 (n=320)	
Other neuropathic pain (Phase 3B) post herpetic neuralgia, sciatica	2 (n=600)	-	-	
Cost (\$ million)	<u>01</u> 6.1	<u>02</u> 59.6	<u>03</u> 55.7	<u>Total</u> 121.4

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ABT 0002370

ABT-594

Phase 2 to 3 Transition

Milestone review	6/01
End of Phase 2 package/request	9/01
Start manufacture Phase 3 supplies	9/01
Ship first Phase 3 supplies	2/02
Initiate Phase 3	3/02
Regulatory filings	9/03

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ABBT 0002371

ABT-594

Overview

First-in-class

- Analgesic potential demonstrated at 75 mcg BID
- Dizziness (7%), nausea (15%), vomiting (5%) observed at 75 mcg BID
- Full efficacy not determined
- MTD is 300 mcg BID
- Phase IIb in painful diabetic neuropathy, using doses up to 300 mcg BID ongoing
- Global sales: \$700 MM

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ABBT 0002372

ABT 594 PROJECT REVIEW

February 2, 2001

PHARMACEUTICAL PROFILE

Jim Sullivan

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ABT 0002373

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P's Exhibit EL

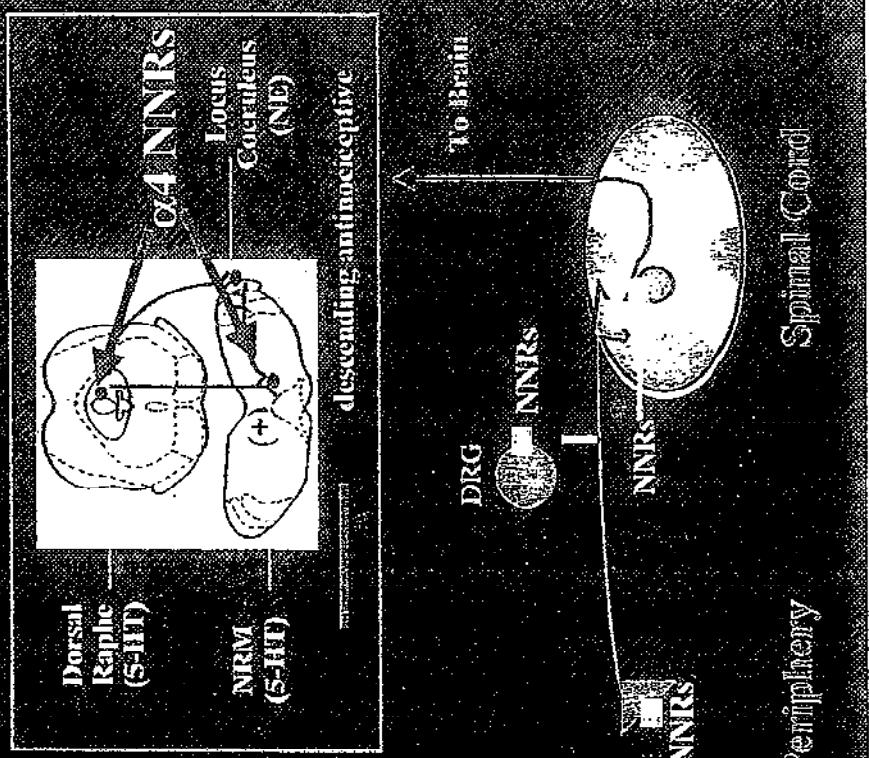
Part 7

ABT-594: Preclinical Pharmacology

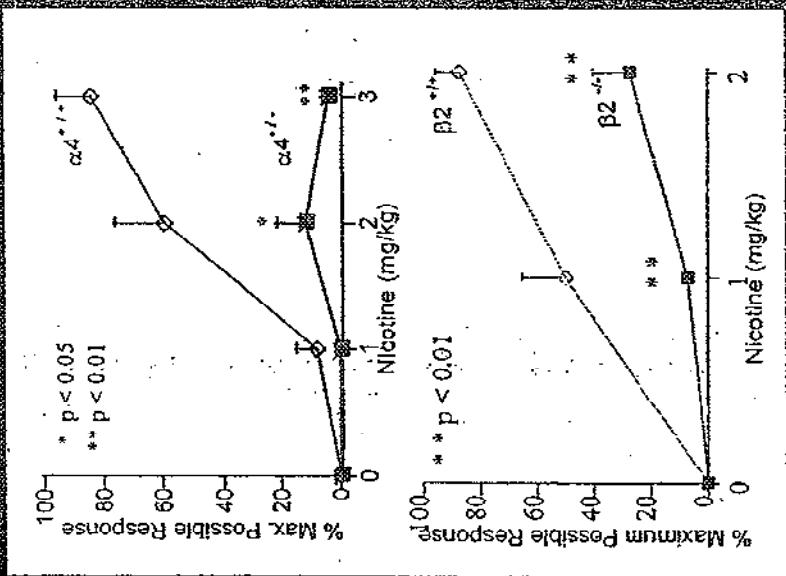
- Rationale for NNRs and pain
 - Knockout, antisense and pharmacological validation
- *in vitro* and *in vivo* profile of ABT-594
 - Efficacy
 - Safety

NNRs and Pain NNRs are Expressed in Pain Pathways

- CNS
 - $\alpha 4$ NNRs are localized in NRM and dorsal raphe (Key CNS pain center)
 - NNRs are expressed in dorsal horn neurons (Key spinal cord pain processing center)
- Spinal Cord
 - $\alpha 4$ NNRs are expressed in dorsal horn neurons (Key spinal cord pain processing center)
- Sensory Neurons
 - $\alpha 4\beta 2$, $\alpha 3\beta 4$, $\alpha 7$ NNRs are expressed in DRG and on central and peripheral C-fiber nociceptors



NNRs FOR PAIN: Role of $\alpha 4$ and $\beta 2$ NNRs Established Using Knockout Mice



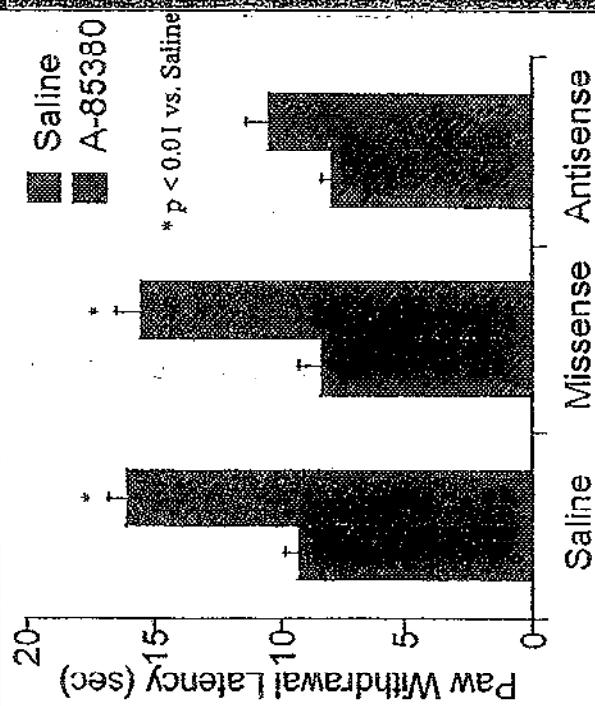
- In either $\alpha 4^{-/-}$ or $\beta 2^{-/-}$ mice, neither nicotine nor epibatidine was active in the hot plate assay (supraspinal mechanism)

Marubio, et al. Nature 1999 398, 805-810

NNRs for Pain: Target Validation Using α 4 Antisense

α 4 Antisense Treatment Attenuates Antinociception in the Hot Box Model of Acute Thermal Pain

- Rats received either a saline, missense, or antisense continuous i.c.v. infusion (0.75 nmol/hr) for 7 days



Bitner, et al. *Brain Res.* 871: 66, 2000

Target Validation

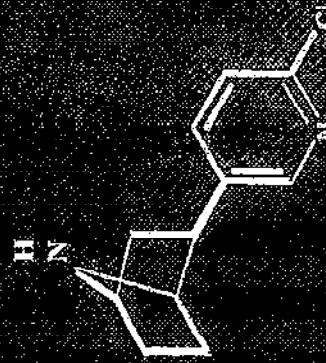
NNR Agonists Are Analgesic

- NNR agonists are -

- Antinociceptive (capable of raising nociceptive thresholds in naïve animals)
- Antihyperalgesic (capable of reversing the reduction in nociceptive thresholds following injury)

- Epibatidine (key discovery)

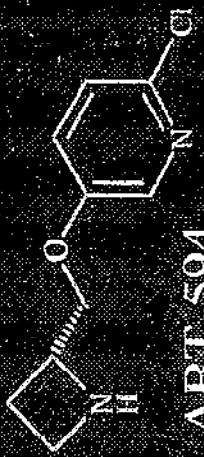
- 200x more potent than morphine
- Non-opioid
- Potent NNR agonist
- BUT highly toxic



Radio and Daily Mol. Pharmacol.
45: 563, 1994.

NNRs and Pain: ABT-594

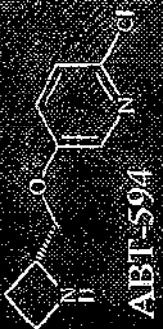
Goal



- Maintain broad spectrum analgesic efficacy of epibatidine
- Maintain potency at $\alpha 4$ containing NNRs
- Decrease side-effect liabilities by decreasing activity at
 - Neuromuscular junction nicotinic receptors ($\alpha 1\beta\delta\gamma$)
 - Ganglionic NNR subtypes ($\alpha 3\beta 4, \alpha 3\alpha 5\beta 2\beta 4$)

ABT-594 is a More Selective NNI¹ than Epibatidine in Radioligand Binding Studies

Binding Site (Ki, nM)	Epibatidine	ABT-594
Cytisine Binding Site (α4β2)	0.042	0.037
BTX Binding Site (Peripheral) (α1)	2.4	16,600



- ABT-594 retains potency of epibatidine at the α4β2 binding site
- ABT-594 is > 5000-fold less potent than epibatidine at the peripheral neuromuscular junction nicotinic receptor

In Vitro Functional Profiles of ABT-594 and Epibatidine

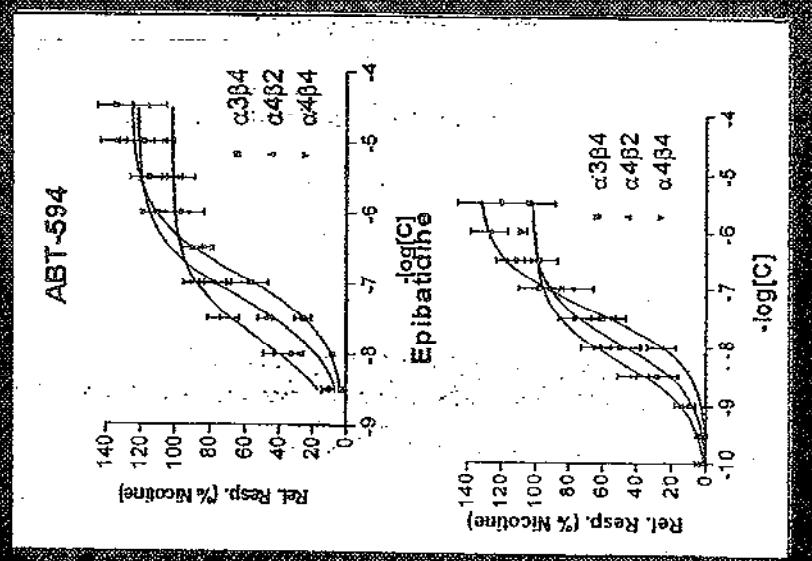
Functional Activity

Rank order of potency

- ABT-594: $\alpha 4\beta 4 \sim \alpha 4\beta 2 > \alpha 3\beta 4$
- Epibatidine: $\alpha 4\beta 4 \sim \alpha 3\beta 4 \sim \alpha 4\beta 2$

ABT-594 displays modest $\alpha 4$ vs $\alpha 3\beta 4$ selectivity

- Compounds with greatly improved selectivity have been identified

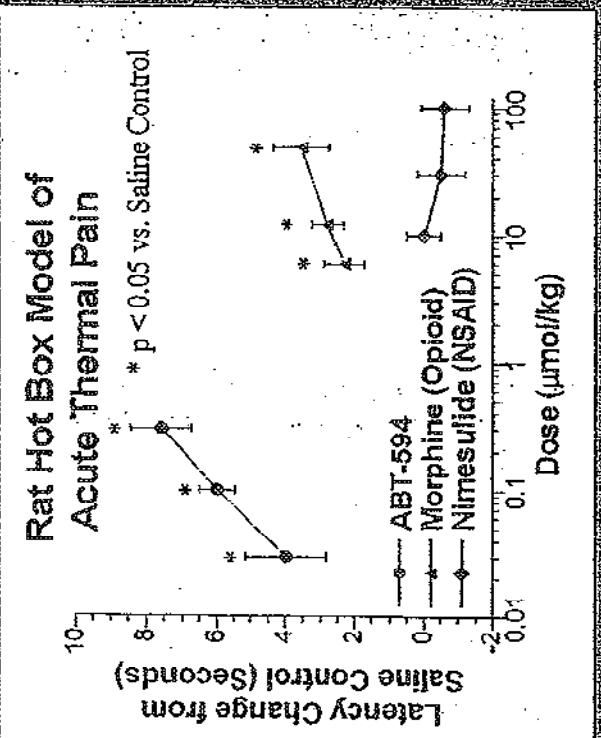


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ABBT 0002381

ABT-594 In Vivo Efficacy in Models of Acute Thermal Pain

- ABT-594 is potent and efficacious in the Hargreaves Hot Box model of thermal nociception
- Onset of Efficacy = < 30 min
- Duration of efficacy ~ 2 hrs
- The effects of ABT-594 are blocked by the nicotinic antagonist mecamylamine, but not by the opioid antagonist naloxone

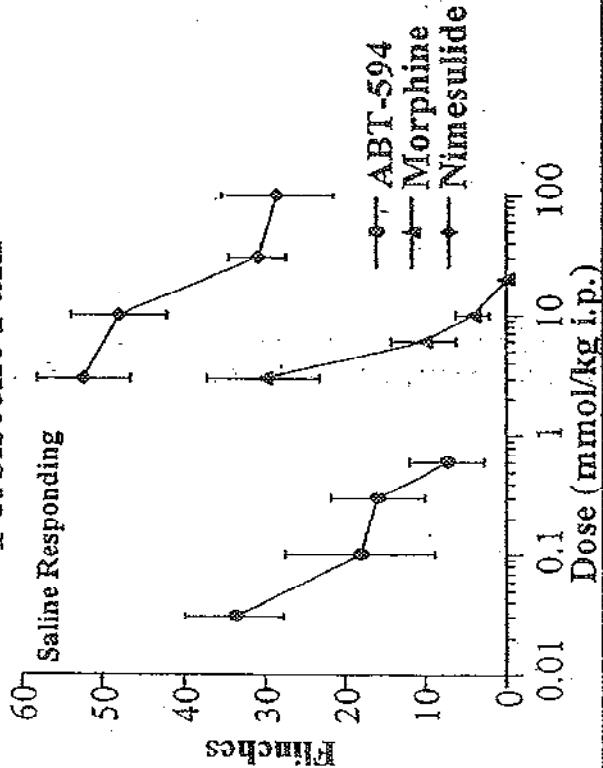


ABT-594 In Vivo Efficacy in Model of Persistent Pain

ABT-594 exhibits comparable efficacy and 50-fold greater potency than morphine in Phase II of the formalin model of persistent chemical pain

ABT-594 is active upon both i.p. and oral administration

Rat Formalin Model of Persistent Pain



Landsberg Deposition Exhibit 28

P's Exhibit EL

Part 8

Classification of Pain

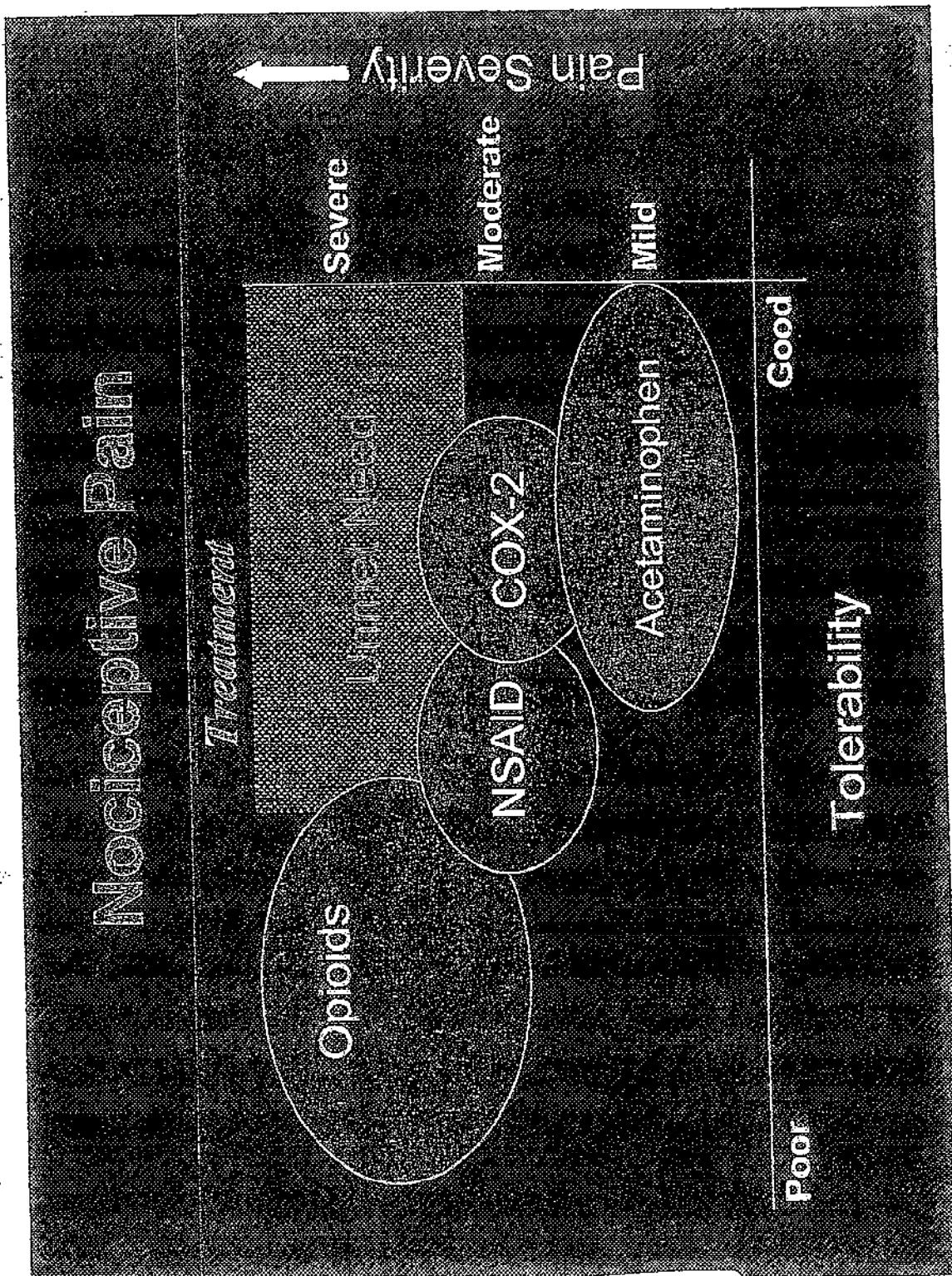
Pain Epidemiology

Chronic pain

- 20% U.S. population: any chronic
- 22% Worldwide: persistent pain

Neuropathic pain

- 20% of diabetics
- 40% of HIV infected
- 36% of cancer



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NOCICEPTIVE PAIN

Treatment Adverse Events

**Ultram¹
50-100 mg**

OxyContin²

**OxyContin
Osteoarthritis
20 mg q12**

Event	Ultram ¹ 50-100 mg	OxyContin ² Osteoarthritis 20 mg q12
Somnolence	N/A	23 %
Dizziness	31 %	13 %
Nausea	34 %	23 %
Vomiting	13 %	12 %
Constipation	20 %	22 %
Pruritis	N/A	N/A

¹Chronic non malignant pain up to 30 days (label)

²Clinical trials (label)

N/A - Not Available

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Neuropathic Pain

Overview

Characteristic Symptoms

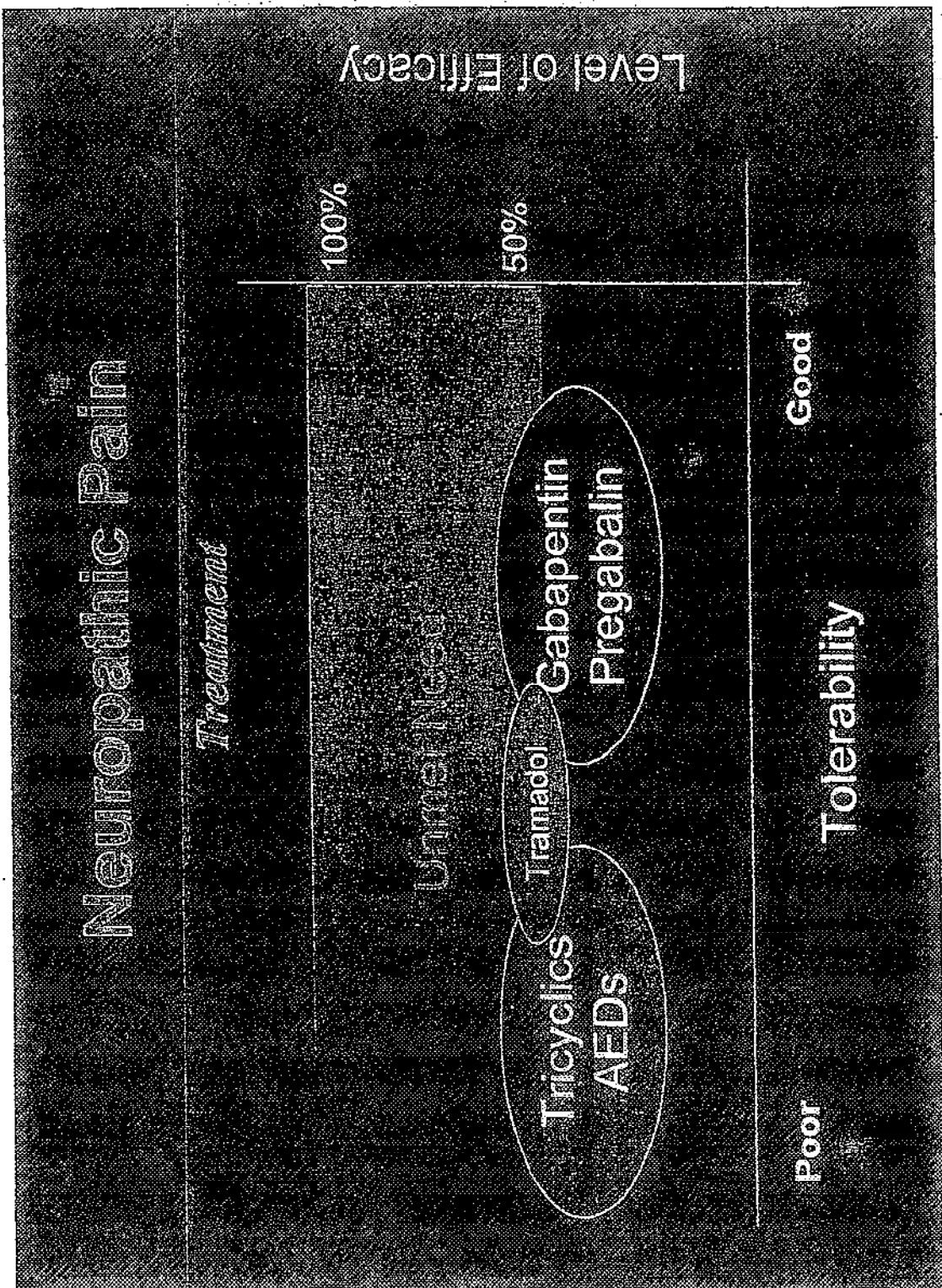
- Spontaneous: dysesthesia, shooting pains
- Evolved: allodynia, hyperpathia

Pathophysiology

- Associated with peripheral nerve injury
- Abnormalities develop over time in the PNS and CNS

Treatment

- Tricyclic and other "antidepressants"
- Antiepileptic drugs
- Sodium channel blockers (lidocaine)
- Opioids
- All minimally effective



Neuropathic Pain

Treatment Adverse Events Rates

Event	Amitriptyline 150 mg/d ¹	Carbamazepine 600 mg/d	Gabapentin 3600 mg/d	Pregabalin 300 mg/d
Confusion	N/A	N/A	5%	5%
Somnolence	66%	53%	23%	24%
Dizziness	28%	40%	24%	27%
Nausea	N/A	7%	8%	N/A
Peripheral edema	N/A	N/A	N/A	7%
Dry mouth	90%	N/A	N/A	N/A
Instability	N/A	13%	N/A	N/A

¹ Max 1987 (n=29)
N/A - Not Available

ABT-594

Clinical development

- Current pain management
- Development strategy: bench to bedside
- Clinical trial results

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ABT-594

Proof of Principle

What characterizes an innovative analgesic?

Spectrum of activity

Time of onset/duration

Level of efficacy

Safety/efficacy ratio

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ABT 504

Specifying off Acuity. Where to Start?

Acute

Post-dental surgery
Sprains and strains
Acute back pain
Trauma
Post-general surgery
Post-orthopedic surgery
Dysmenorrhea
Renal colic
Biliary colic
Pancreatitis
Infections

Neuropathic

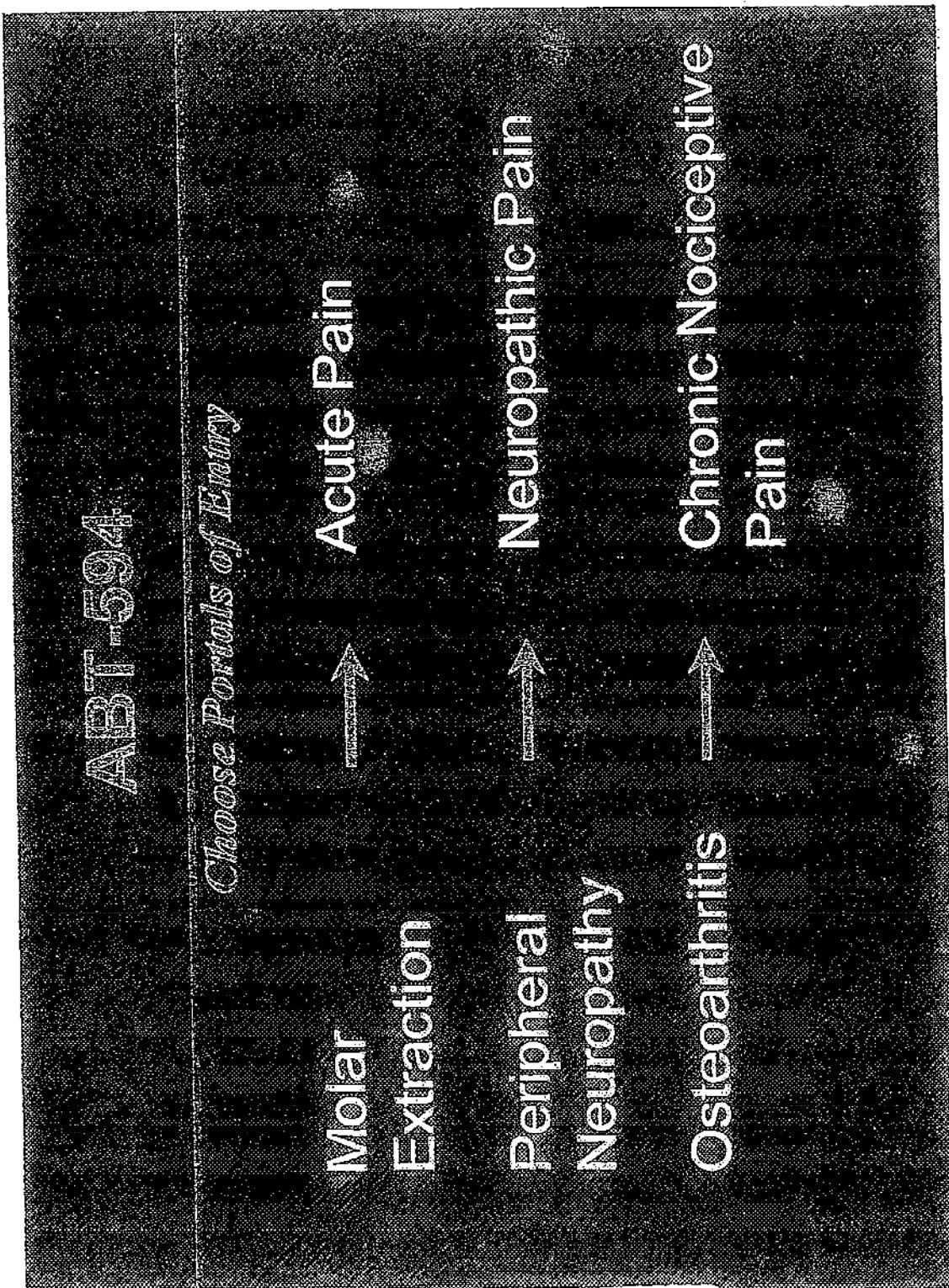
Diabetic polyneuropathy
Idiopathic polyneuropathy
Alcoholic polyneuropathy
Drug-induced polyneuropathy
HIV predominantly sensory neuropathy
Back pain
Cancer pain
Trigeminal neuralgia
Post-herpetic neuralgia
Thalamic pain syndromes
Spinal cord injury
Multiple sclerosis
Complex regional pain syndromes (C.R.P.S.)
Atypical facial pain
Phantom limb pain

Chronic Nociceptive

Osteoarthritis
Chronic back pain
Rheumatoid arthritis
Cancer pain
Fibromyalgia
Sickle cell disease
TMD disorder
Bursitis
Tenitis
Chronic visceral pain

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Landsberg Deposition Exhibit 28

P's Exhibit EL

Part 9

ABT-504

Initial Profile

Preclinical promise

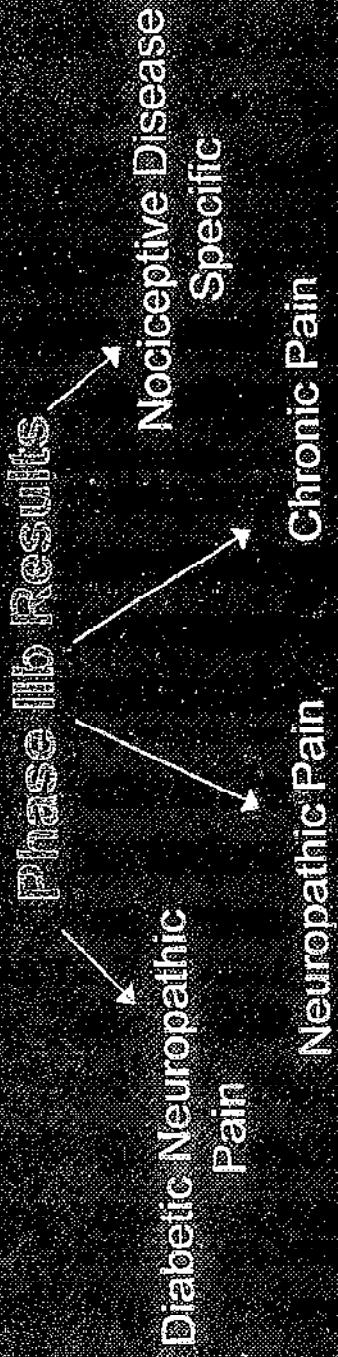
- Efficacy for all types of pain
- Challenges

Current characteristics

- Analgesic potential demonstrated in molar extraction, neuropathic pain and osteoarthritis
- Onset (T_{max} ; tolerability) appears to exclude rapid relief of pain ("acute pain")

ABT-594

Future Regulatory Strategy



+/- Publication Strategy/Phase IV (e.g.)

- Postherpetic neuralgia
- Nociceptive pain
 - o Osteoarthritis
 - o Low back pain

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ABT-594

Clinical development

- Current pain management
- Development strategy: bench to bedside
- Clinical trial results

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ABT-594

Pharmacokinetics and Metabolism

- Half-life ($t_{1/2}$): about 8-12 hours

- Dose proportional kinetics

- AUC, C_{max} similar across formulations (solution, SEC, HGC)
- AUC, C_{max} similar with/without food
- T_{max} varies somewhat with formulation, food

No clinically significant effects on cytochrome P450 isoforms

- Elimination primarily through renal excretion, about 50% unchanged drug recovered in urine

ABT-594

ABT-594's analgesic potential demonstrated in:

Molar Extraction

Neuropathic Pain

Osteoarthritis

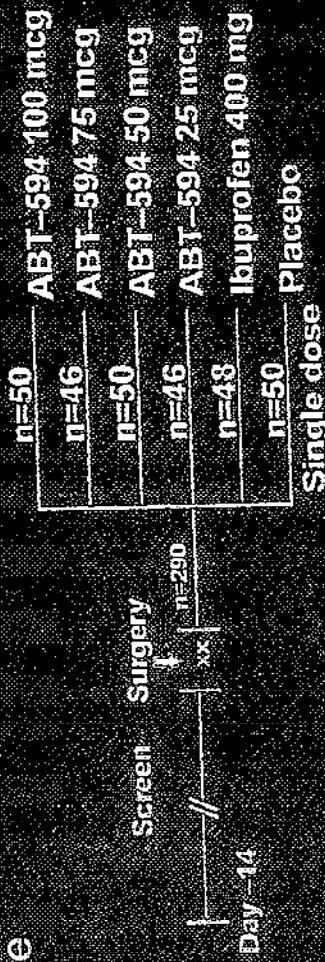
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ABT 0002408

Molar Extraction Study

Design

290 patients, randomized, double-blind, placebo-controlled, single dose



- Third molar extraction
- Outcome measures:
 - Pain relief (PR)
 - Categorical scale:

0	1	2	3	4
none	a little	some	a lot	complete
- Power: 70% to detect an effect similar to acetaminophen plus Codeine Solution

Molecular Extraction Study

ONICOTHE MUSUMES

Pain Relief (PR)
Categorical scale:

0	1	2	3	4
none	a little	some	a lot	complete

Total Pain Associated Relief (TOTPAR)

Area under the curve for PR (0-6 hours)

Pain Intensity (P)

Categorical scale

Visual Analog Scale

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Stop Watch Model – Time to "perceivable" and "insensitive" Time To Rescue Medication

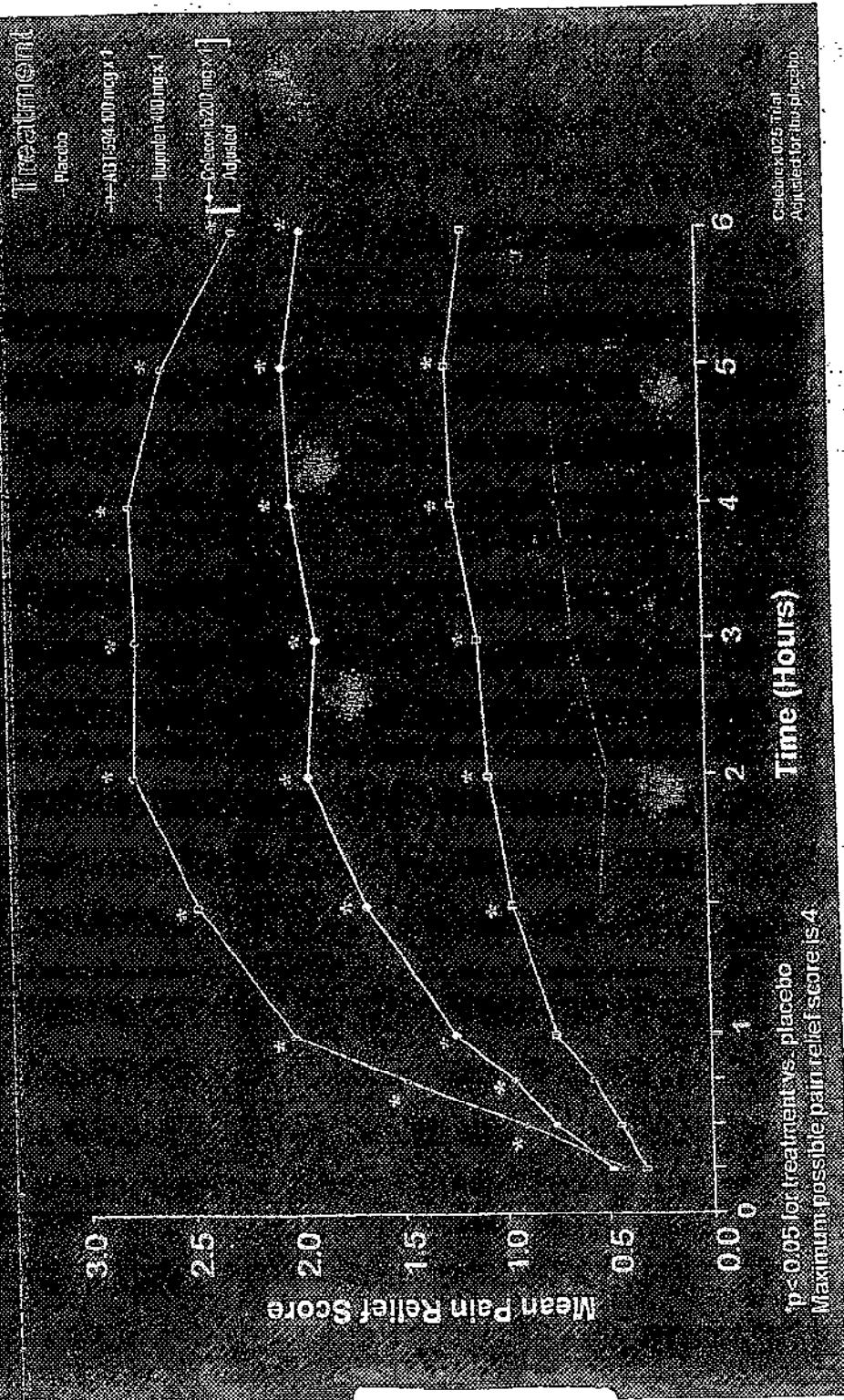
111

A vertical scale with four horizontal tick marks. Above the first tick mark is the number '1'. Above the second tick mark is the word 'fair'. Above the third tick mark is the word 'good'. Above the fourth tick mark is the word 'excellent'. The numbers 1, 2, 3, and 4 are positioned to the left of the scale, aligned with the tick marks.

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ABT-594 100 mcg Is Significantly Better Than Placebo Starting 4.5 Hours After Dosing



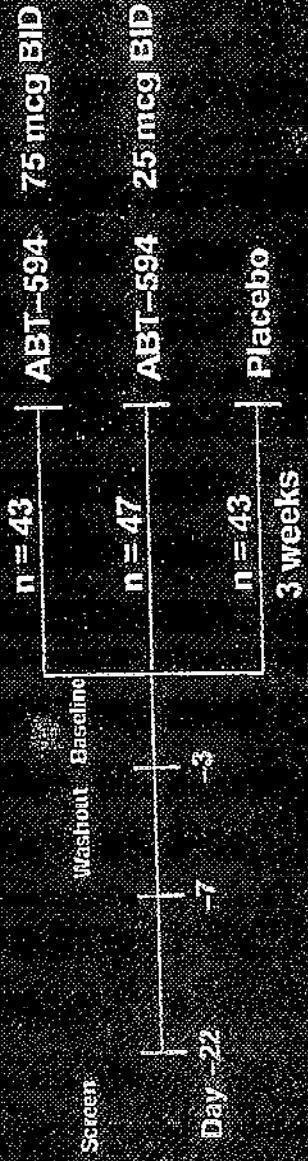
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Neuropathic Pain Pilot

Design

- 133 patients, randomized, double-blind, placebo-controlled, multiple dose



- Distal symmetric polyneuropathy
- 52% idiopathic
- 46% diabetic
- Power: 56% to detect a 20% difference (ABT-594 vs. placebo)
- Soft Elastic Capsule

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Technische Raumplanung

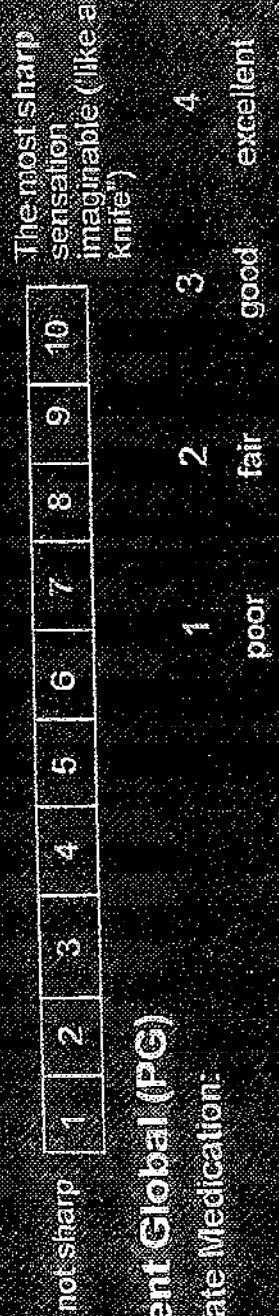
Outcome Measures

Pain Intensity (P1)

- Categorical Scale:
- Visual Analog Scale (0-100 mm)

Neuropathic Pain Scale (NPS)

– 10 items (e.g., sharp, hot, intense) for total 0-100 points
Please use the scale below to tell us how **sharp** your pain feels. Words used to describe "sharp" feelings include "like a knife," "like a spike," "stabbing" or "like jolts."



Patient Global (PC)

Patient Global (PC)

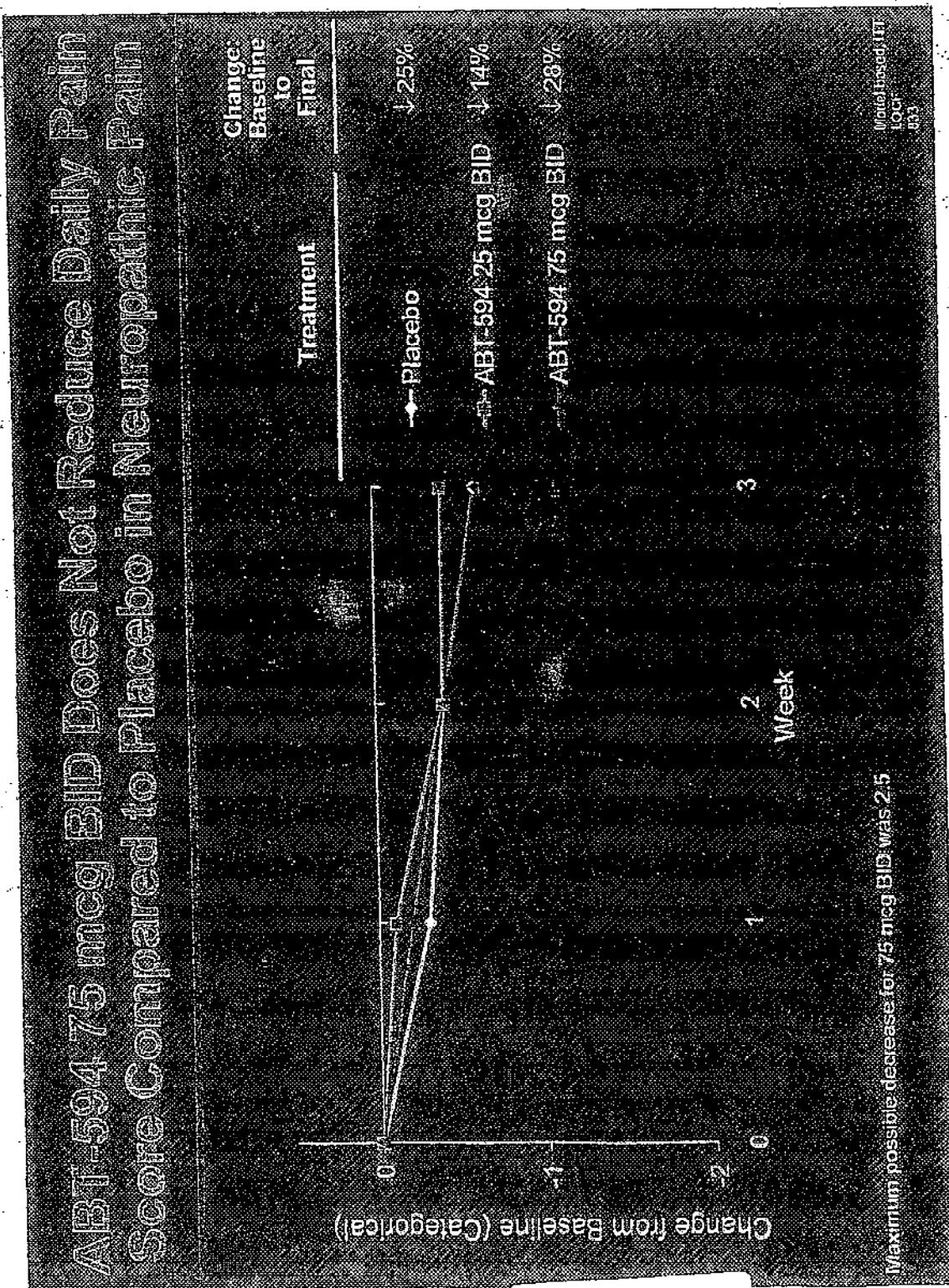
Rate Medication:

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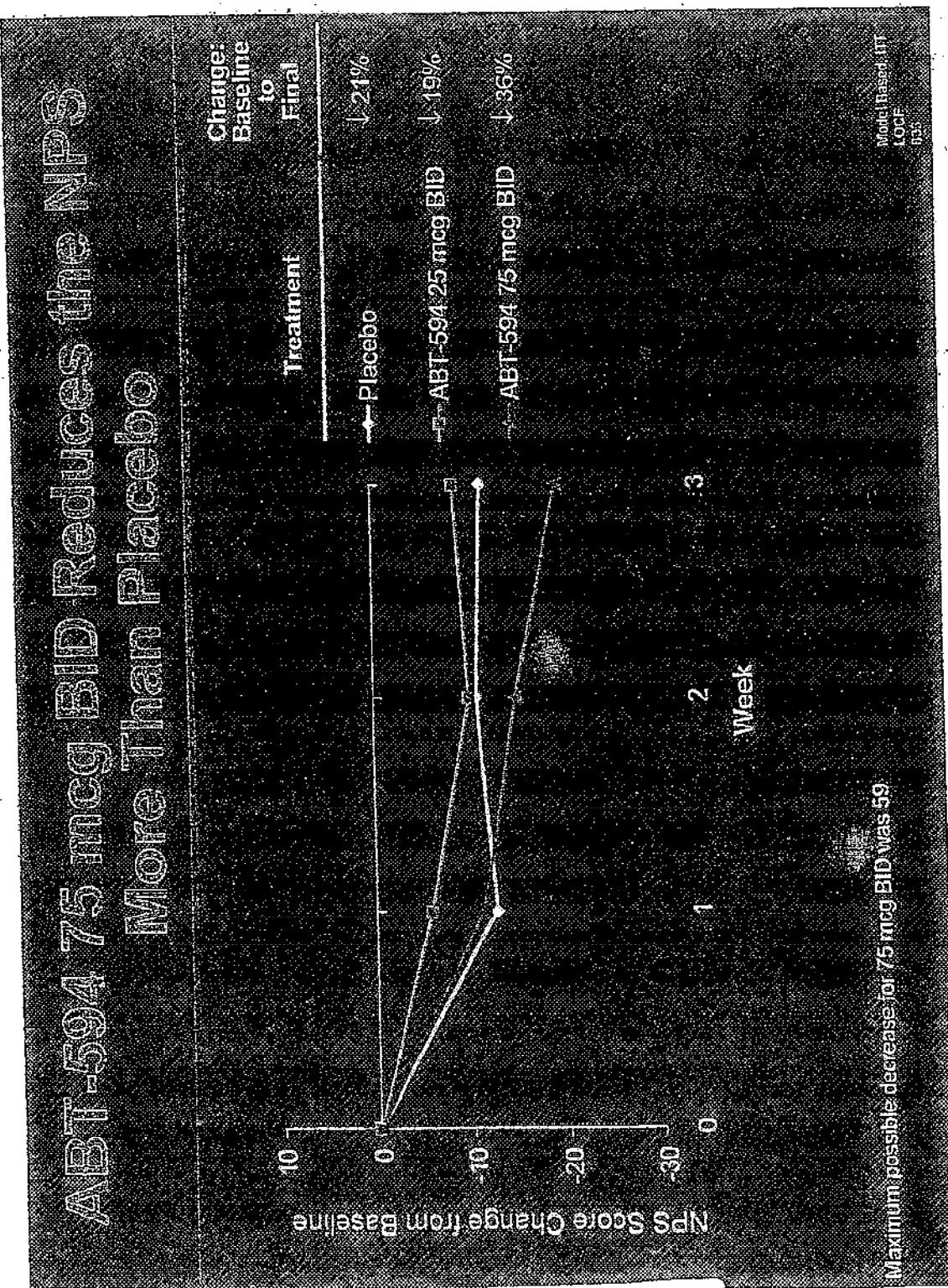
Landsberg Deposition Exhibit 28

P's Exhibit EL Part 10



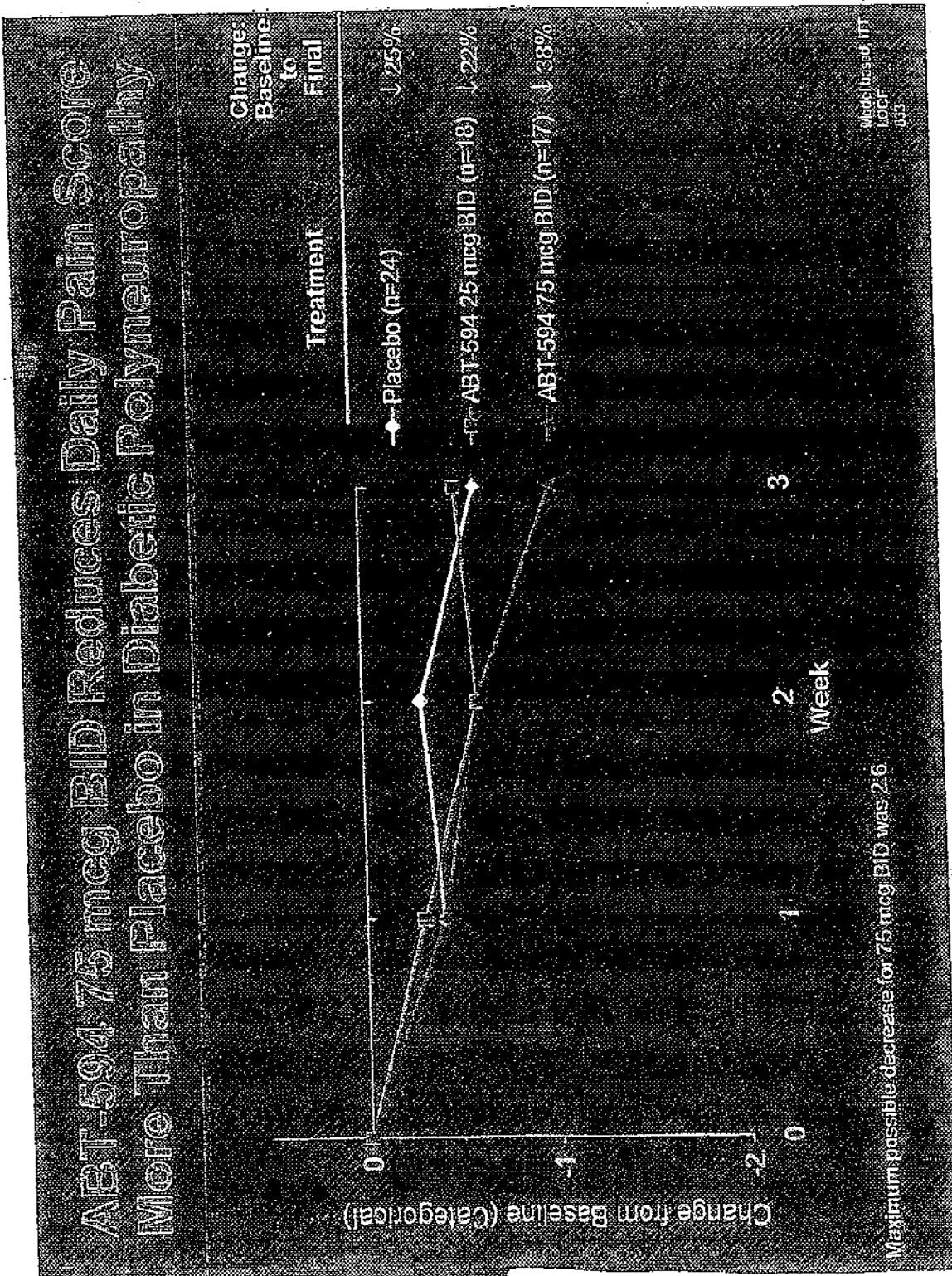
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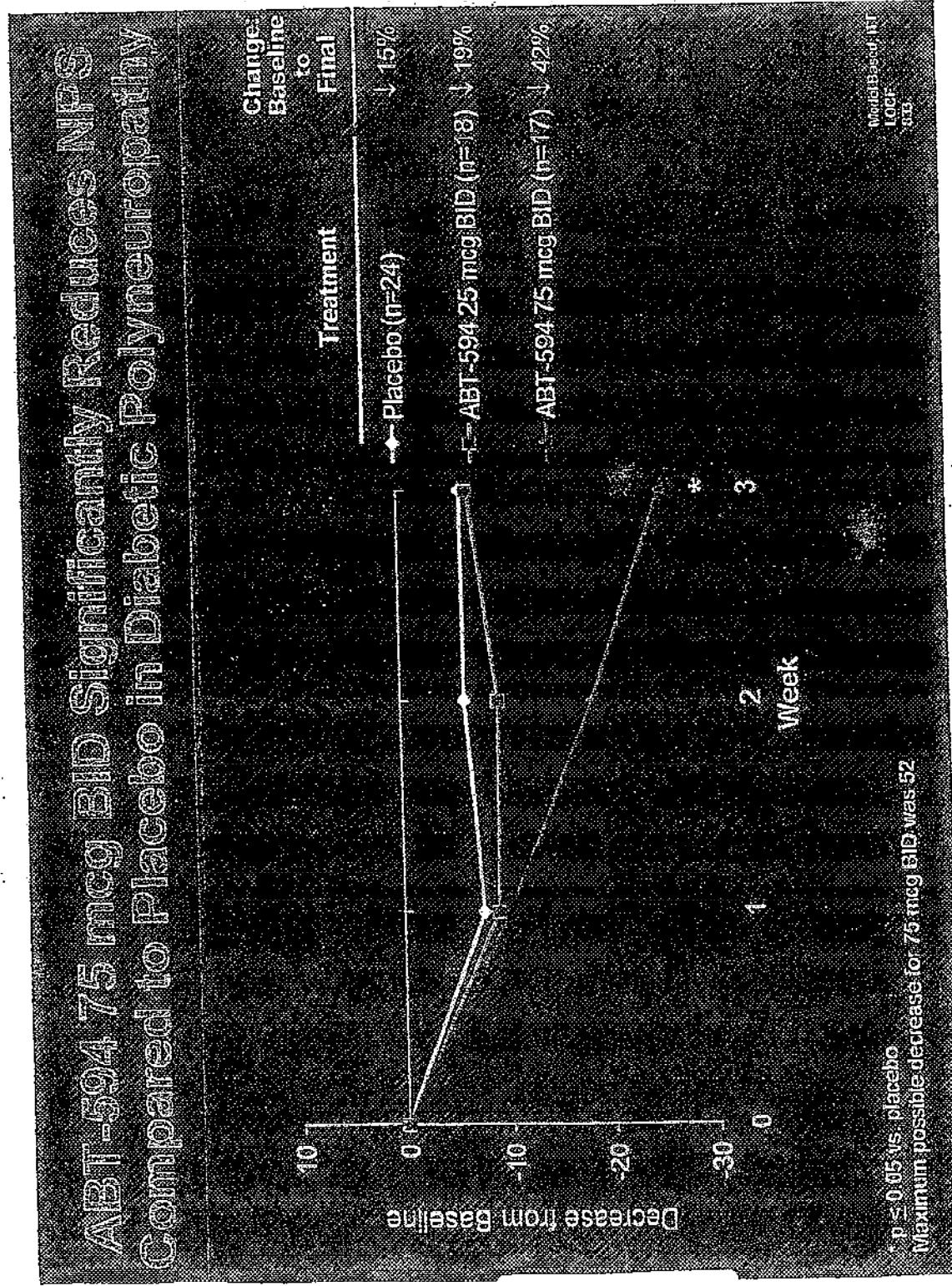
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ABBT 0002416



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ABBT 0002418



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ABT 0002417

ABT-594 75 mg Q BID has a Similar Effect To Gabapentin

ABT-594 vs. Gabapentin and Pregabalin



14 point categorical scale (1 vs. baseline
21 point Likert Scale Week 8 vs. baseline
31 point Likert scale week 5 vs. baseline

Expected Clinical Dose
Pregabalin
Diabetes

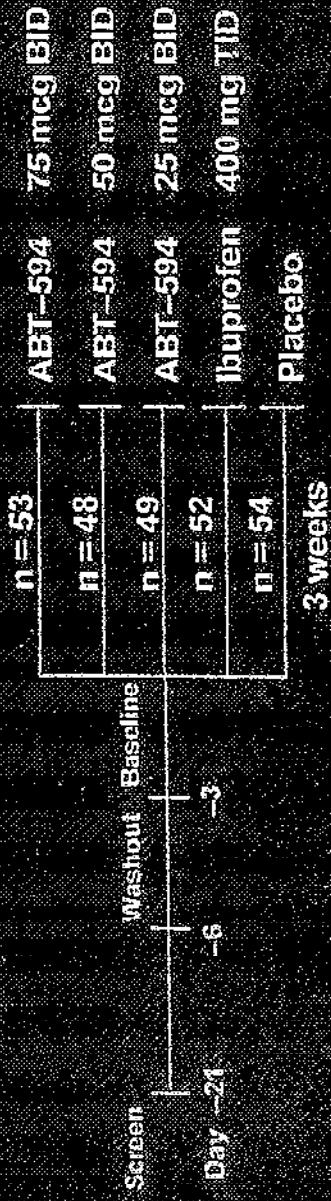
Highest Effective Dose
Gabapentin²
(Diabetes)

Lowest Effective Dose
ABT-594
Diabetes

Osteoarthritis Pain Pilot

Design

- 256 patients, randomized, double-blind, placebo-controlled

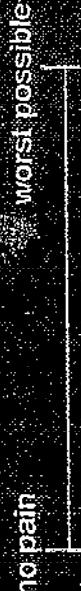


- Power: 56% to detect a 20% difference (ABT-594 vs. placebo)

- Soft Elastic Capsule

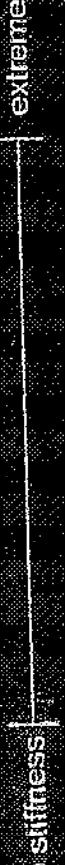
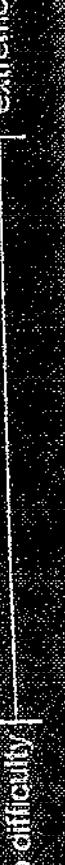
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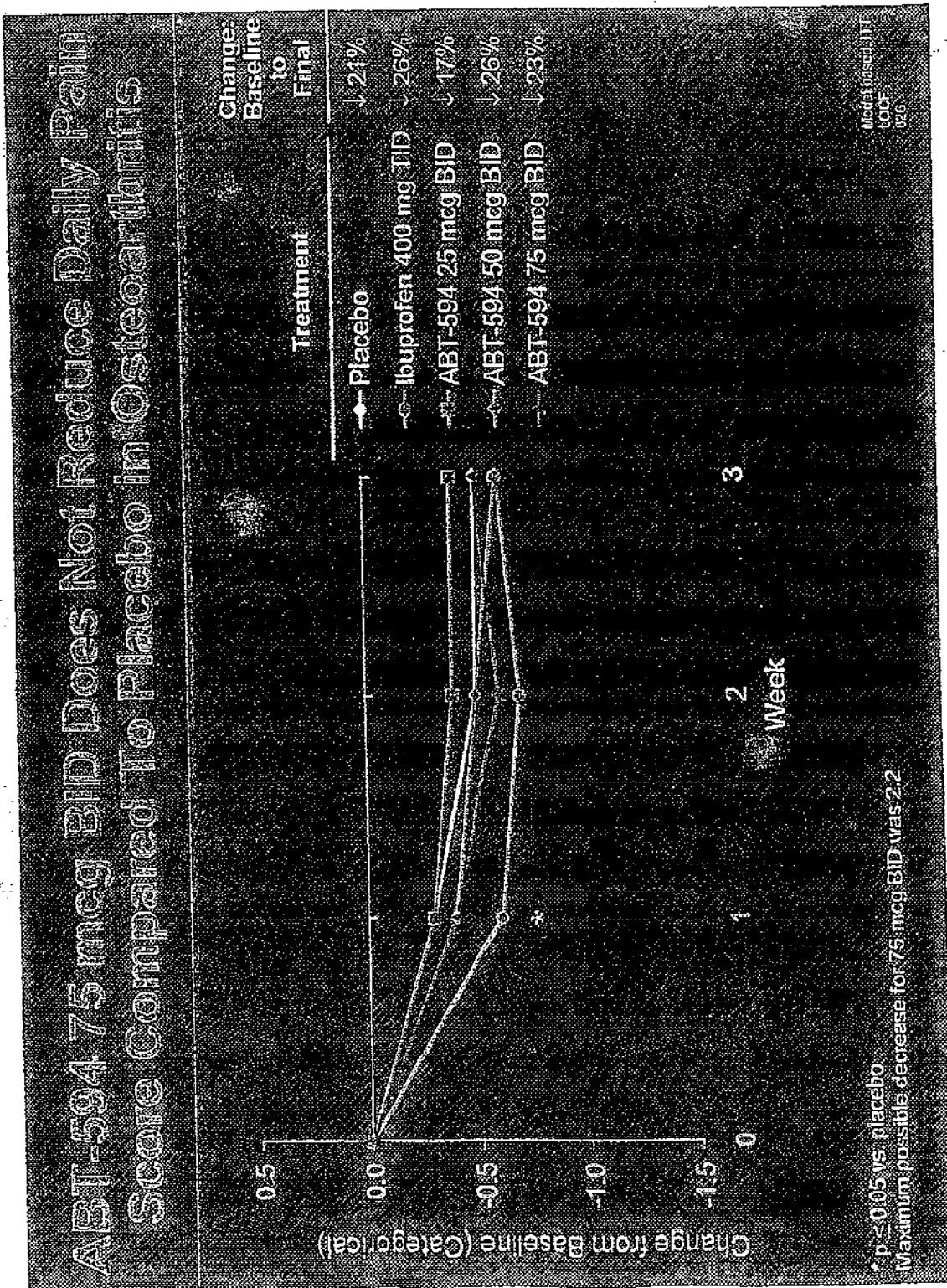
ABT 0002418

Outcome Measures	
Pain Intensity (P) - Categorical Scale:	3 2 1 0 none mild moderate severe
- Visual Analog Scale (VAS):	
	
WOWAC - Pain (0-500) - Stiffness (0-200) - Function (0-1700) Total (0-2400)	
Patient Global - Rate Medication:	4 3 2 1 poor fair good excellent

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ABBT 0002420

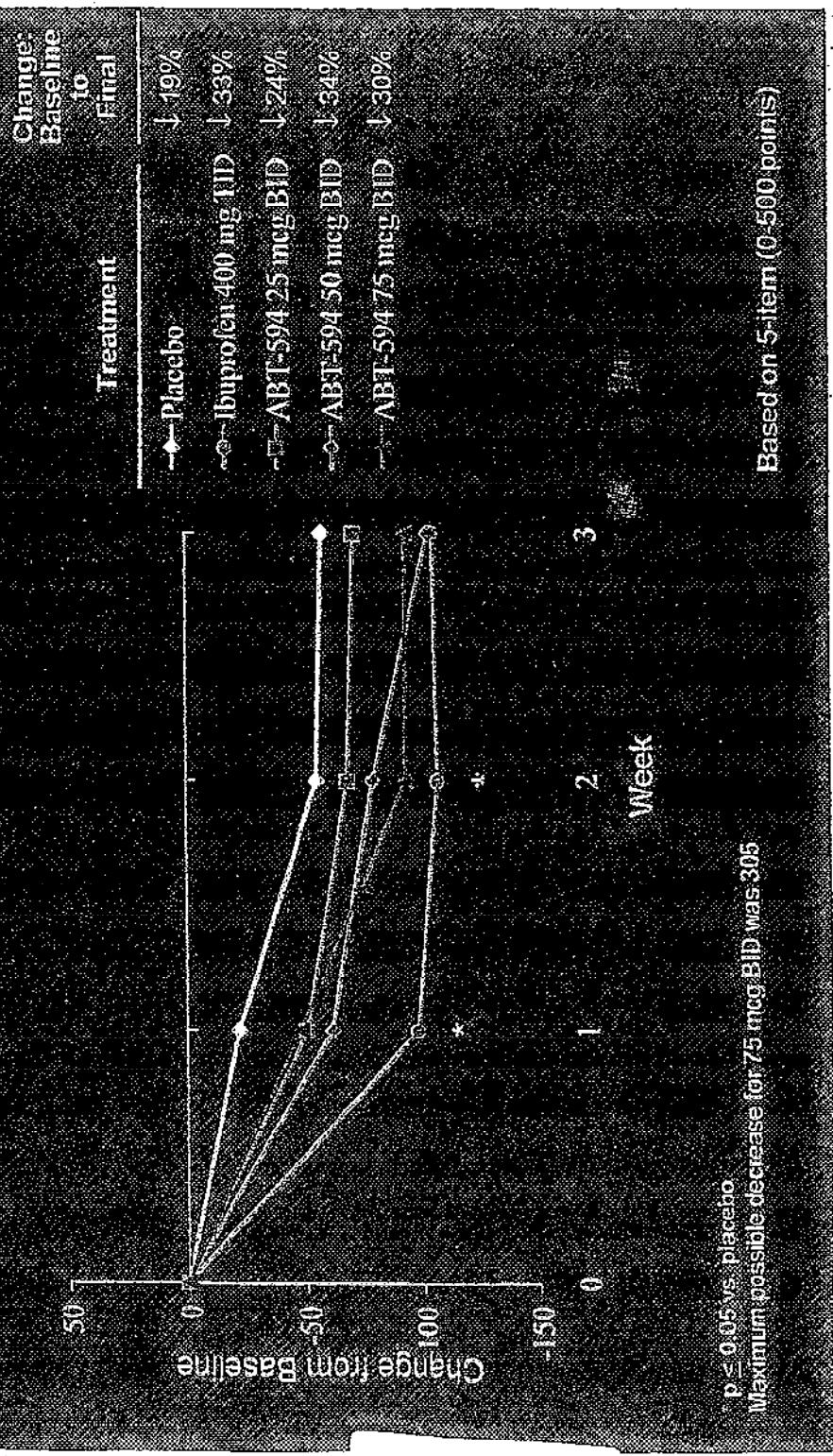
Osteoarthritis Pain Pilot Study	
WOMAC	
Pain	How much pain do you have...
	<ul style="list-style-type: none">— Walking on a flat surface?— Going up or down stairs?
	 no pain extreme pain
Stiffness	How severe is your stiffness...
	<ul style="list-style-type: none">— After sitting, lying, or resting later in the day?
	 no stiffness extreme stiffness
Function	What degree of difficulty do you have...
	<ul style="list-style-type: none">— Descending stairs?— Rising from bed?
	 no difficulty extreme difficulty



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ABST 0002422

ABT-594 75 mcg BID Reduces the WOMAC Point Subscale More Than Placebo in Osteoarthritis

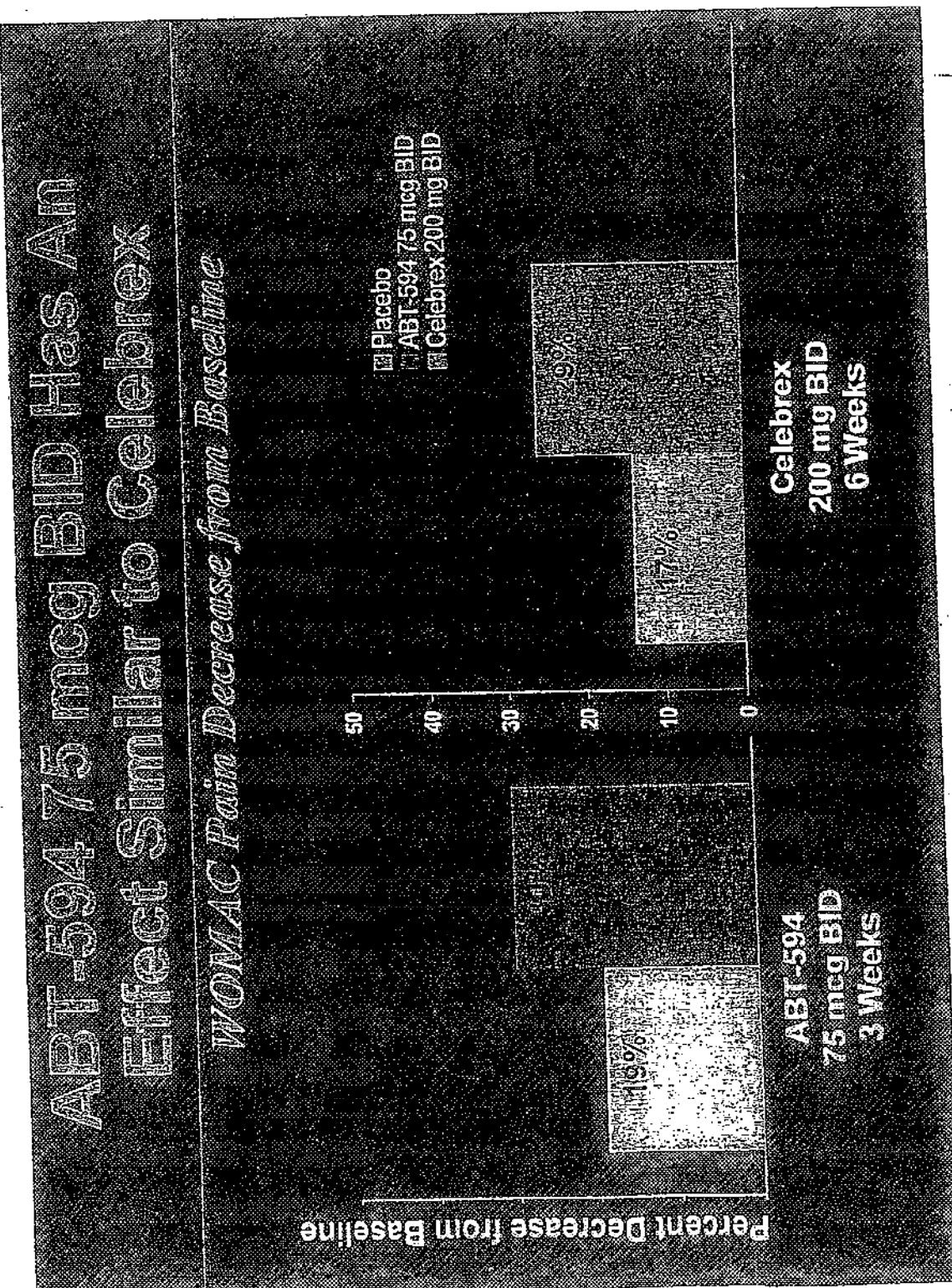


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ABBT D002423

Landsberg Deposition Exhibit 28

P's Exhibit EL Part 11



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ABT-504

Phase III Efficacy Conclusions

Analgesic Potential Demonstrated

- Molar Extractions
 - Significance vs. placebo starting at 1.5 hours
- Neuropathic Pain
 - 75 mcg BID may be lowest effective dose for patients with painful diabetic polyneuropathy
- Osteoarthritis Pain
 - 75 mcg BID may be lowest effective dose as judged by the WOMAC pain sub-score

ABT-594 Safety

Phase III Adverse Events

Characteristic AES

- Nausea
- Vomiting
- Dizziness

AES attenuate after repeated administration

Adverse Event Rates for Selected Antidepressants

Event	Amitriptyline 150 mg/d	Carbamazepine 600 mg/d	Cabapentin 3600 mg/d	Pregabalin 300 mg/d	ABT-594 75 mcg BID
Confusion	N/A	66%	N/A	6%	5%
Somnolence	66%	53%	23%	21%	11%
Dizziness	28%	40%	20%	27%	7%
Nausea	N/A	N/A	N/A	N/A	N/A
Vomiting	N/A	N/A	N/A	N/A	N/A
Peripherial edema	N/A	N/A	N/A	N/A	14%
Constipation	N/A	N/A	N/A	N/A	20%
Diary incontinence	N/A	N/A	N/A	N/A	N/A
Instability	N/A	N/A	N/A	N/A	N/A

¹ Max 1987 (n=29)
² M96-925 and MGB-823 combined
 N/A Not Available

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Adverse Event Rates for Select Analgesics

Event	Ultram ¹ 50-100 mg q4-6h	Oxy/Contin ² 20 mg q12h	Oxy/Contin Osteoarthritis 20 mg q12h	ABT-534 ³ 75 mcg BID
Somnolence	N/A	23 %	27 %	0 %
Dizziness	31 %	13 %	20 %	7 %
Nausea	24 %	22 %	41 %	15 %
Vomiting	13 %	12 %	25 %	5 %
Constipation	38 %	23 %	32 %	1 %
Dry mouth	N/A	N/A	N/A	49 %
Furitis	N/A	N/A	N/A	N/A

¹ Chronic non-malignant pain, up to 30 days (label)

² "Clinical trials" (label)

M98-026 and M98-343 combined

N/A - Not Available

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ABT-594

Phase IIa Conclusions

- Analgesic potential demonstrated
- Phase IIa studies included inadequate dose ranging

- SEC tolerated better than predicted by solution
- 75 mcg BID (HGC) very well tolerated vs. other analgesics
- Two Phase I studies (M99-076 and M99-120) showed:
 - 300 mcg BID HGC tolerated
 - Titration may improve tolerability

- Full analgesic potential should be defined with adequate dose ranging studies in Phase IIb

Phase III

Trials

- Neuropathic Pain (M99-114)
 - Ongoing
- Osteoarthritis Pain (M99-115)
 - Unfunded

Doses

- 150, 225, 300 mcg BID

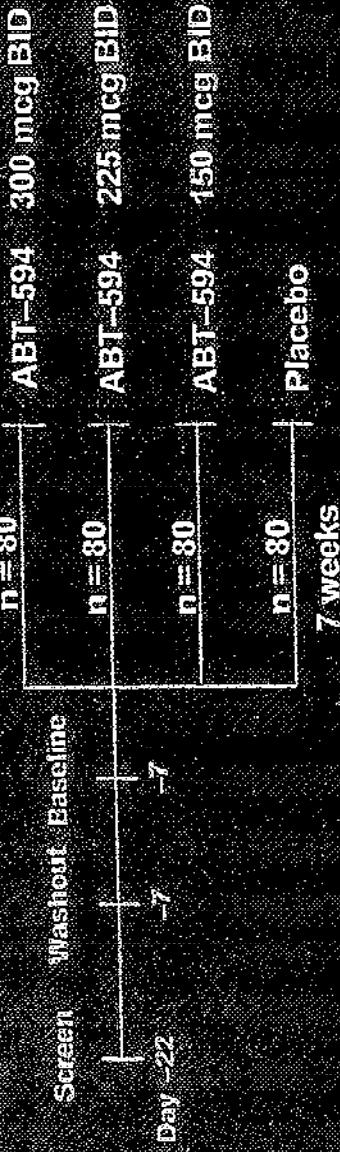
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ABT-594 Neuropathic Pain

Design

320 patients, randomized, double-blind, placebo-controlled, multiple dose



Diabetic polyneuropathy

- 7-Day primer phase, treatment visits at 2, 3, 5 and 7 weeks
- Power: 80% with 0.05 Type I to detect 39% ABT-594 improvement, 25% placebo (ES 0.46)
- Hard Gelatin Capsule

MOQ-114: Neuropathic Pain

Outcome Measures

Primary

- Weekly average of daily pain (11-point Likert in a diary)

Secondary

- Site-based pain scale (11-point Likert)
- Neuropathic Pain Scale
- Patient Global Impression of Change
- Physician Global Impression of Change
- SF-36

MO9-114 Status

- Enrollment
 - Ended 1/5/01 at 269 subjects
 - Pre-specified power not reached
 - Width of confidence intervals not meaningfully different between 269 and 320 enrolled
- Database release – 5/01
- Go/No Go – 6/01

Landsberg Deposition Exhibit 28

P's Exhibit EL Part 12

ABT-594

Take Home Messages

1. Significant unmet needs in pain management

2. Prior studies: Potential of ABT-594 to address these unmet needs

3. On going study: Test the hypothesis that ABT-594 addresses unmet need in neuropathic pain

— A proposed study would do the same for chronic nociceptive pain

4. There is a process by which we will determine if ABT-594 can satisfy the unmet need

ABT-594 Project Review

February 2, 2001

Commercial Assessment

Andrea Landsberg

Laura Robinson

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ABT-594 Commercial Assessment

Key Take Aways

- Neuropathic pain market is the primary target
 - Underserved market with significant unmet need
 - ABT-594 has potential to be first novel drug in decades indicated for neuropathic pain
- Additional opportunity in “Chronic persistent pain” market
- Key challenge is achieving optimal balance of tolerability and efficacy to satisfy both US and ex-US markets

Neuropathic Pain Market Sales		2000 US Sales (\$MM)	2000 ex-US Sales
AEDs	\$299	\$190	\$45
TCAs	\$3	NA	NA
OPIOIDS	\$37	\$45	\$280
OTHERS	\$85	\$424	
TOTAL			

US Sales / factored for neuropathic pain and annualized
Vs Prior Year: US Growth est 20%, ex-US Growth est 10%

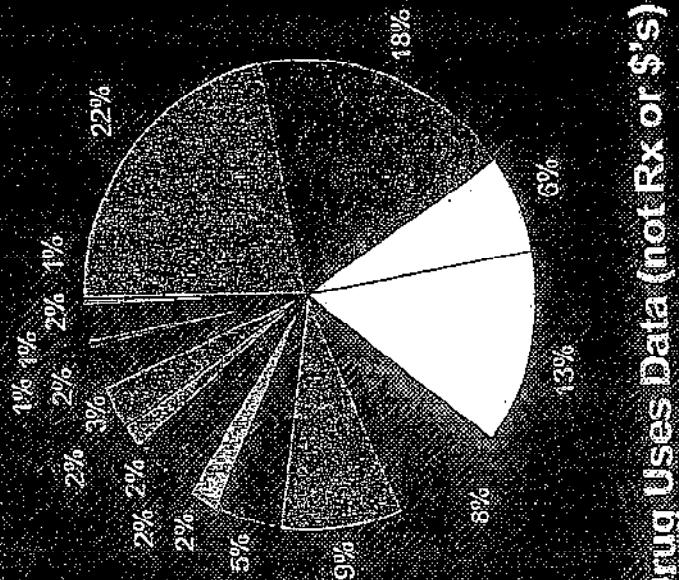
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Drug Classes Used to Treat Neuropathic Pain

Dispersed market due to limited promotion and lack of dominant effective product

SEIZURE DISORDERS
ANTIDIARRHEICS SYS/PIN
COX-2 INHIBITORS
CODEINE & COMB NON-INJ
CORTICOIDS PLAN/INJ
ANTIDEP TRIVETRA
PTY ANALGESICS
PYRIDOXINE (VIT B6)
SYN/NON-NARC NON-INJ
MUSC RELX W/O ANALG
CORTICOIDS PLAN/ORAL
PROPOXYPHENES
ANESTH INJECT/LOCAL
ASPIRIN, ACETIC
SSRIS/SNRIS
ACETAMINOPHEN
BENZODIAZEPINES



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Usage in Neuropathic Pain

- Even if target only 'focused' indication in 'painful, diabetic neuropathy' expect trial and usage in all types of neuropathic pain
- Neurontin use all off-label
- Carbamazepine is indicated for trigeminal neuralgia but used in all neuropathic pain
- Generally held premise that NIP likely has some similar mechanisms across etiologies (reinforced by current drug usage)

Market Opportunities in Neuropathic Pain

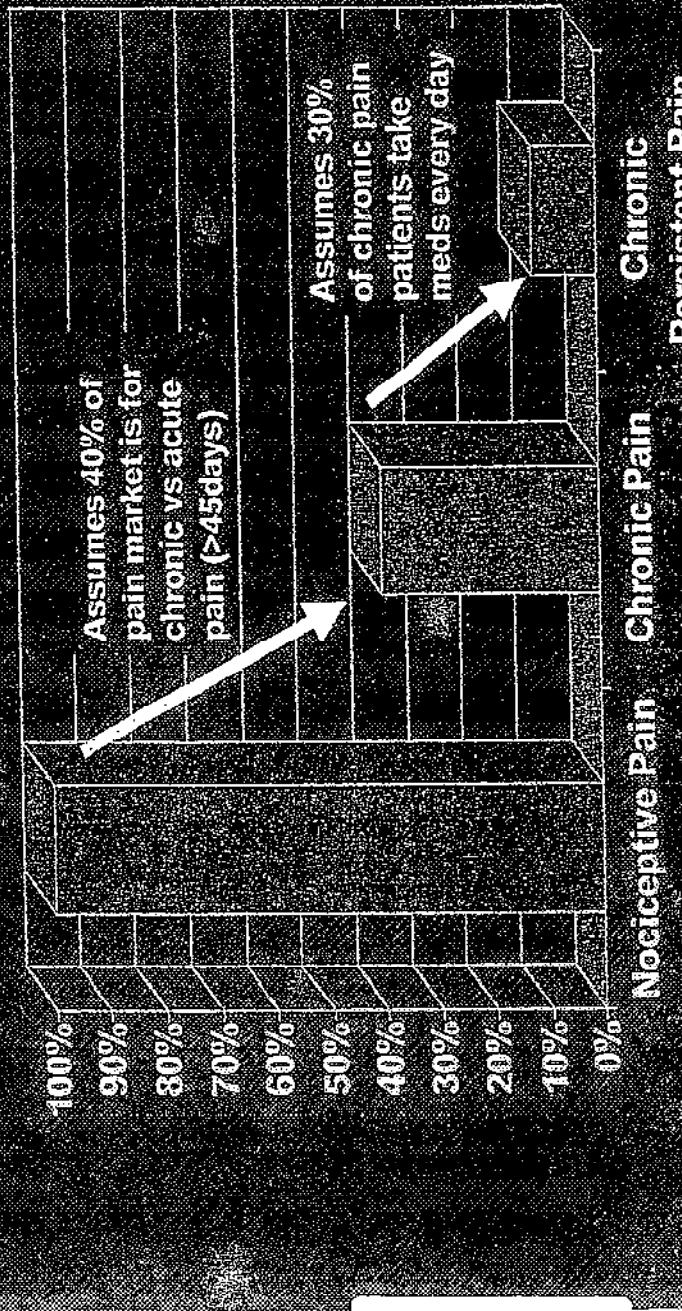
- Improved efficacy
 - Partial pain relief is the norm
 - Polypharmacy often required to manage pain
 - Improved responder rates
 - Typically only 40% to 60% of patients respond to any given treatment
- Improved tolerability over time
 - TCAs, AEDs, opioids have troublesome SEs that do not diminish over time
 - Dose reduction
- Most TCAs and AEDs (including Neurontin) typically dosed TID
- Titration reduction
 - TCAs and AEDs require >2 weeks titration period to minimize SEs or reach effective dose

Chronic Persistent Pain (CPP)

Spinilove®

- Onset of action and need for titration limits ABT-594 to a small segment of the nociceptive pain market
- CPP = Chronic persistent pain conditions for which patients are on daily medications over extended periods of time (vs. PRN, or 'as needed' consumption)

Chronic Persistent Pain



IMS Longitudinal Data indicates over 30% of pain meds Rxed for >=30 days
Quantitative primary market research indicates that >60% of chronic pain patients take meds every day

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Chronic Pain Market

1999 Sales (\$MM)	CAGR (97-99)	Rxs (MM)	CAGR (97-99)
US \$700	5%	35	1%
Ex-US \$680	8%	58	3%

GPIP Market Size Assumptions:

Assume 40% of opioid, non-opioid, COX-2 market is for chronic pain care
30% of that is 'persistent', i.e., medication taken every day

Landsberg Deposition Exhibit 28

P's Exhibit EL

Part 13

Qualitative Market Research Results

Profile	Share of Patients		
	OA	RA	Low-back
Efficacy	AEs vs Current agents		

Assumes ABT-594 is indicated for MP, with additional clinical data
(Ph II) showing efficacy in nociceptive pain

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ABBT 0002444

QUICKTIV[®] Market Research Results

Profile		Share of Patients		
Efficacy	AEs vs. current agents	OA	RA	Low-back
Better	Equivalent			
Same	Equivalent			
Better	Poor			

TCAs used as "benchmark" efficacy in NP

Tolerability vs. current agents: equivalent = 5% nausea, 5% vomiting; 10% dizziness; poor = 20% nausea; 10% vomiting; 30% dizziness

Qualitative Market Research Results

Profile		Share of Patients		
Efficacy	AES vs current agents	OA	RA	Low-back
Better	Equivalent	19%	12%	16%
Same	Equivalent	15%	8%	10%
Better	Poor	12%	6%	11%

Spillover market share in chronic persistent pain markets (in forecast, assuming only 5% share)

MR did not test impact of variation on market share

Qualitative Market Research Results		Share of Patients	Neuropathic Pain
Efficacy	Profile		
Better	AES vs. current agents	Equivalent	31%
Better		Poor	24%
Same		Equivalent	27%

Assumes ABT-594 is indicated for NP, with additional clinical data (T7/11) showing efficacy in nociceptive pain
In forecast assuming 20% share of NP

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NEUROPATHIC PAIN PIPELINE

- Pregabalin is in Phase III, but questions remain regarding Pfizer's Neuronitin/Pregabalin strategy
- 4 N/NR preclinical programs appear to be targeting pain indications; ABT-594 is much further along
- Other new AEDs may have potential for treatment of neuropathic pain and are conducting phase IV trials; unclear whether these agents will pursue an NP indication
- Several novel pain mechanisms being explored
 - Calcium channel blockers
 - Sodium channel blockers
 - NMDA antagonists

Positioning of ABT-594 in Neuropathic Pain

- Greater efficacy than AEDs and TCAs in NP
- Better long term tolerability (than TCAs and opioids)
- Safe in all patient populations
- Convenient BID dosing with simple, short titration period
- No tolerance over time and non-scheduled
- Limited drug interactions
- Novel mechanism of action

POSITIONING of ABT-594 in CPT

- o Effective alternative to opioids with:
 - No tolerance, respiratory depression, constipation, etc.
 - Non-scheduled
- o For patients receiving insufficient relief with current therapies or NSAID/opioid intolerant patients
- o Better efficacy than COX-2s with novel mechanism of action and no major safety issues

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ABT-504 Global Forecast Ranges

Peak Sales (\$MM)			
	Low	Base	High
US	\$92	\$339	\$506
Ex-US	\$130	\$363	\$712

- NP shares: 5%, 20%, 30%
- CPP shares: 3%, 5%, 7%

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Key Product Challenges

- Key challenge is achieving optimal balance of tolerability and efficacy to satisfy both US and ex-US markets
 - Neurontin/Pregabalin may have advantage
 - Will need to minimize early DCS as much as possible
 - Potentially low therapeutic index
 - Titration
 - Schedule must be as short and simple as possible
 - NICE mechanism
 - Will require pre-launch market education and priming to diffuse negative associations and generate interest surrounding novel MOA

GOV/NO GO PROCESS

Bruce McCarthy

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Landsberg Deposition Exhibit 28

P's Exhibit EL Part 14

ABT-594

Go/No Go Process

The Challenge

Integration of many interrelated data

- Efficacy
- Safety
- Dose Response
- Pharmacodynamics
- Dose Selection
- Phase III Trial Design
- Filtration Effects
- Indications

- Market Research
- Segmentation
- Targeting
- Positioning

The Plan

Leverage decision analysis (DSC) as a process
to determine Go/No Go criteria

ABT-594

Go/No Go Process

Process to include:

1. Scope and frame issues and process
2. Analysis of M99-114 and other clinical data
3. Dose identification
4. Draft Phase III trial design
5. Market research
6. Valuation
7. Presentation and asset strategy: 6/01

Decision Analysis

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Go/No Go Process

What will a "Go" decision look like?

Patients and physicians will have
compelling reasons to choose ABT-594 vs.
other analgesics for the relief of pain

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ABT 594 Project Review

February 2, 2001

Follow-On Strategy

Mike Meyer

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Identification of ABT-594 Backup

Clinical Results Online Specific Improvements Required for Backup

- Emesis
 - Modeled preclinically in ferret and dog
- Nausea
 - Ferret model can qualitatively address nausea index
- Dizziness
 - Mouse rotated
 - Rat Edge test

Discovery Project Basics

NNR Subtypes Differentially Mediate Efficacy and Side Effects

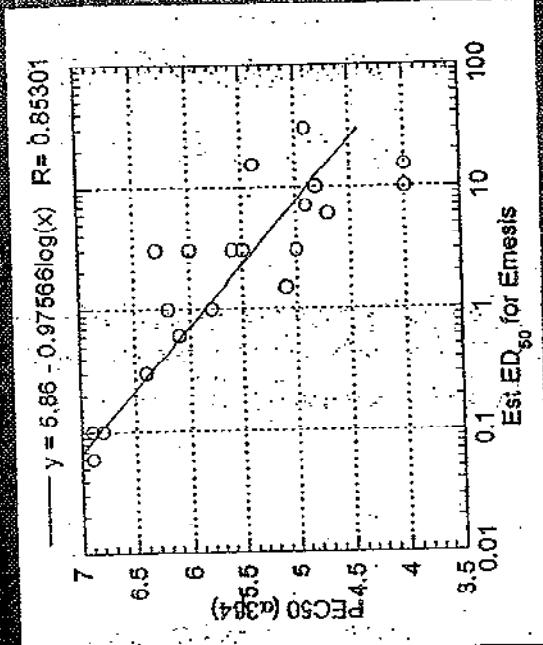
- Different NNR subtypes mediate analgesic effects of nicotinic agonists and adverse events
- Program committed to the identification of NNR subtype selective compounds
- Project initiated research collaboration with NeuroSearch (Denmark)
 - Access to human recombinant NNRs
 - Access to new structural classes of NNR modulators

Nociception Mediated by $\alpha 4$ Subtypes

- Mouse knockouts support role of $\alpha 4$ and $\beta 2$
 - Key differences between pain type
- Role for $\alpha 4$ subtype in acute thermal pain (activation of descending inhibitory pathways)
 - Antisense studies
 - Site injection studies
 - Antagonist studies
- In more physiological relevant models of persistent and neuropathic pain, both central and peripheral sites of action are implicated

Emesis Mediated by $\alpha_3\beta_4$ Subtypes

- In preclinical models, emesis is correlated to potency and efficacy at ganglionic ($\alpha_3\beta_4$) NNR subtypes
- Antagonist and route of administration studies suggest both local and systemic contribution



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Q4-Selective Ligands in Vitro Profile

Radioisland Binding Profile:

0.046 nM 0.049 nM

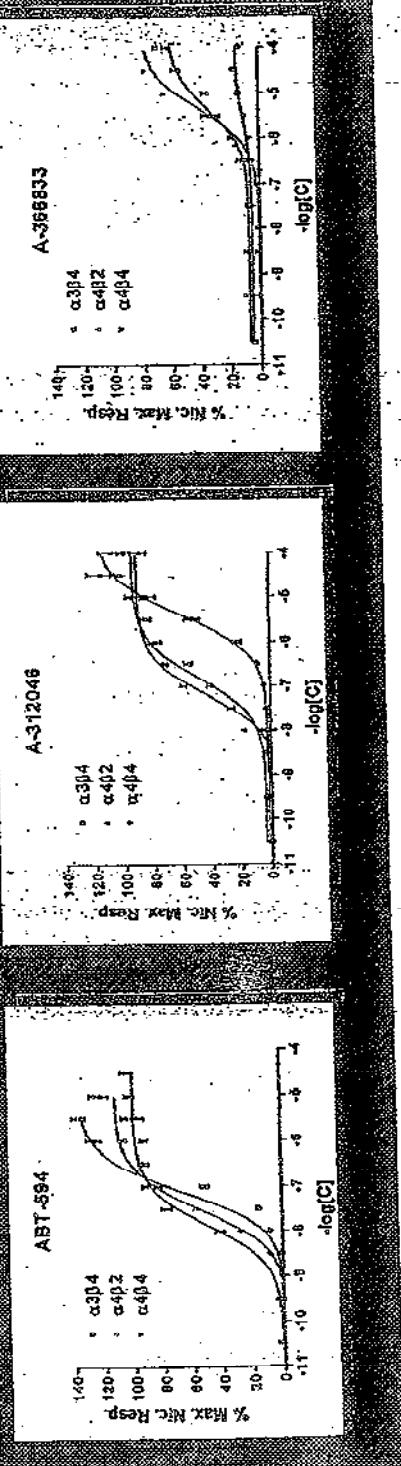
3.19 nm

3.19 nM

A-366833
A-312046

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In Vitro Functional Profile:



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Analgesic Efficacy vs. ABT-594 (Rat Models)

	Persistent Nociceptive Pain (Formalin Model)	Neuropathic Pain (Chung Model)	Acute Nociceptive Pain (Hot Box)
ABT-594	+++ (0.08 μmol/kg)	+++ (0.1 μmol/kg)	+++ (0.03 μmol/kg)
A-312046	+++ (1.8 μmol/kg)	+++ (0.7 μmol/kg)	+++ (1.9 μmol/kg)
A-366833	+++ (3 μmol/kg)	+++ (5 μmol/kg)	++ (6 μmol/kg)
Celecoxib	++ (30 μmol/kg)	+	0
Morphine	+++ (3 μmol/kg)	+++ (10 μmol/kg)	+++ (3 μmol/kg)
Gabapentin	+	++ (100 μmol/kg)	0

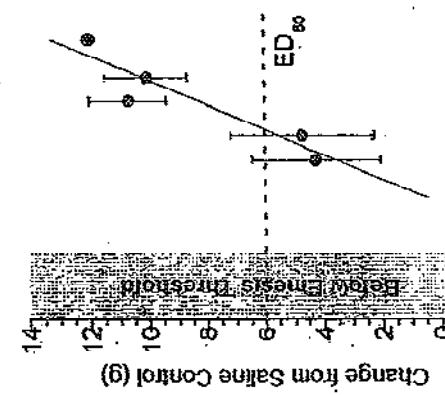
+++ is >75% efficacy, ++ is 40-75% efficacy, + is <40% efficacy, 0 is no activity.

Landsberg Deposition Exhibit 28

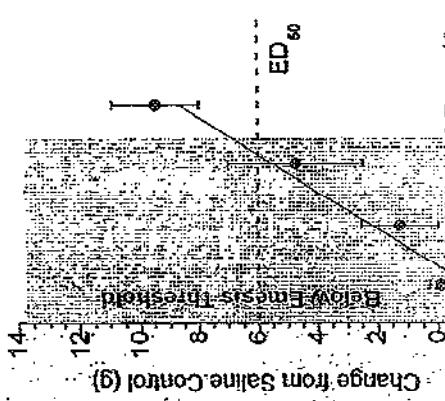
P's Exhibit EL Part 15

Efficacy Indexed to Emesis Liability (Neuropathic Pain)

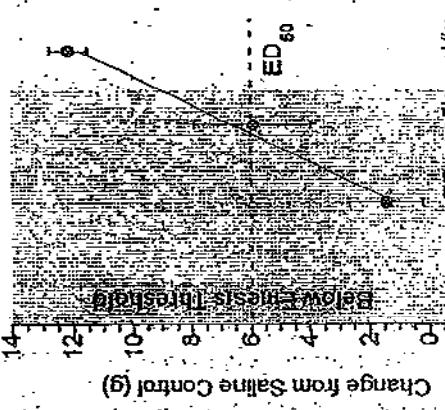
ABT-594



A-312046



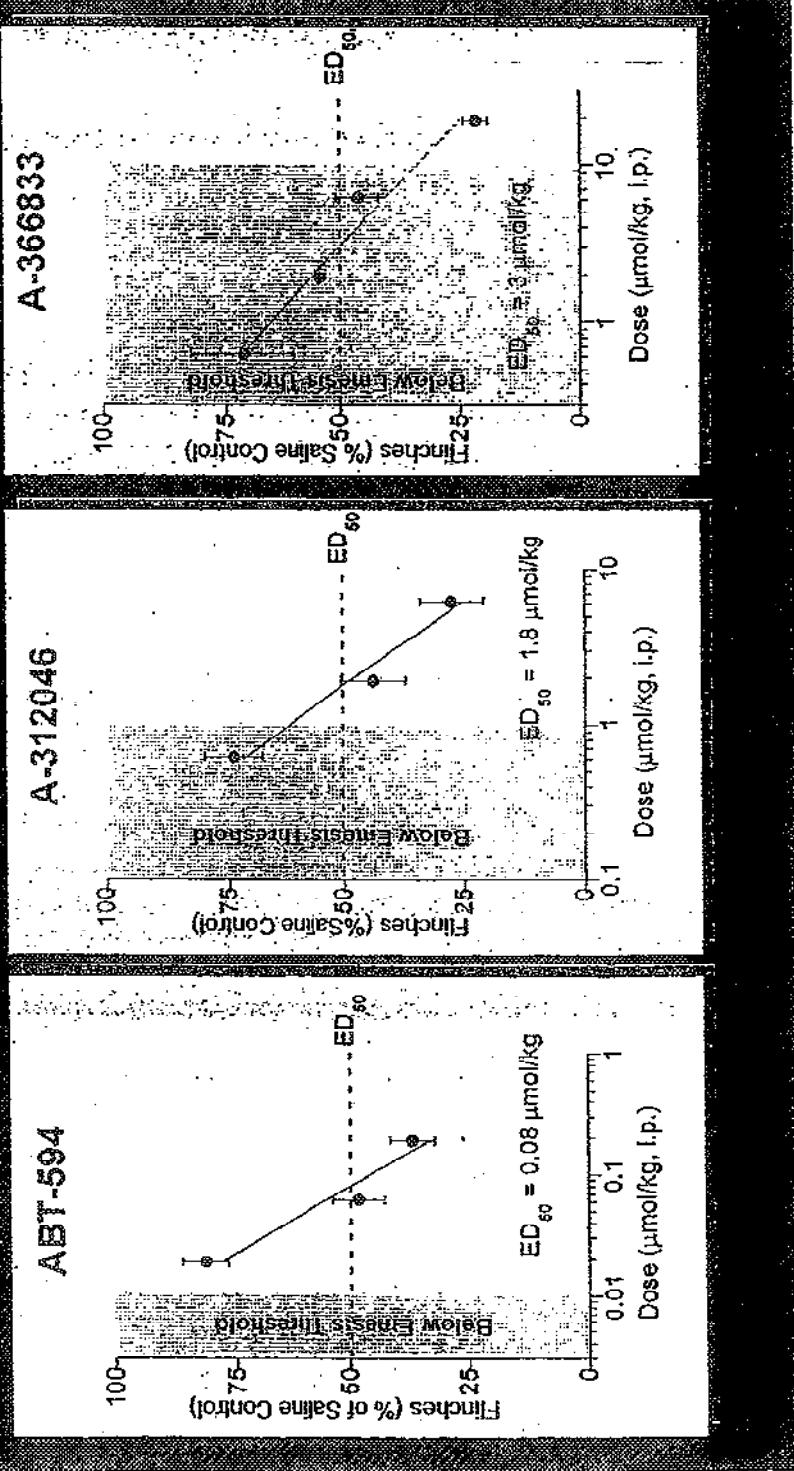
A-366833



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Efficacy Indexed to Femesis Lability (Nociceptive Pain)



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Therapeutic Index Comparison

Therapeutic index based on ratio of highest no effect dose for adverse event and ED₅₀ in pain models

Therapeutic Index	
Improvement vs. ABT-594	
Adverse Event	A-312046
Emesis (Ferret)	5 - 14X
Seizure Threshold (Mouse)	4 - 11X
Edge Test (Rat)	7 - 24X
	20 - 27X
	>11X
	>12X

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Pharmacokinetics

		$t_{1/2}$	CL _p	%F
ABT-594	Rat	1.5 h	1.7	61%
	Dog	4.7 h	0.4	35%
	Monkey	1.4 h	1.7	80%
A-312046	Rat	3.0 h	1.95	30%
	Dog	1.4 h	2.89	13%
	Monkey	1.5 h	2.36	3%
A-3666633	Rat	1.5 h	3.02	73%
	Dog	2.6 h	0.35	100%
	Monkey	2.5 h	0.53	74%

ABT-594

A-312046

A-3666633

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Additional Characterization and Ongoing Studies

- o A-312046:
 - Evaluation of viability of transdermal formulation
 - Identification of prodrug analogs
- o A-366833:
 - Ames and chromosomal breakage neg
 - CEREP binding studies - no significant findings
 - Ongoing studies:
 - o Evaluation in additional pain models
 - o PK/PD studies - plasma levels at efficacious and emetic doses
 - o Dog, monkey, human hepatocyte metabolism
 - o Cardiovascular evaluation
 - o Two-week toxicology in rats

Backup Status

□ A-366833:

- Broad spectrum activity, but particularly effective in persistent nociceptive pain model
- Significantly decreased side effect liability
- Excellent oral bioavailability across three species
- May extend into general pain indication

□ A-312046:

- Excellent activity in neuropathic pain model
- Pharmacokinetics may preclude development as oral drug
- Alternative formulations may be useful as backup for ABT-594 in neuropathic pain market